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TROPICAL DISEASES BULLETIN

IMPERIAL MYCOLOGICAL INSTITUTE
9 JUNE 1943

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Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 40.] 1943. [No. 5.

RECENT MALARIA WORK IN RUSSIA.

By C. A. Hoare, D.Sc.

(*Wellcome Bureau of Scientific Research, London.*)

During the last three years there have appeared in *Medical Parasitology and Parasitic Diseases*—the journal issued in Moscow by the Central Institute of Malaria and Medical Parasitology (formerly the Institute of Tropical Medicine)—a series of papers devoted to various aspects of malaria. The present review deals with some of the papers published in this journal in 1940, 1941 and 1942.

Clinical Findings.

Considerable interest is attached by Russian workers to the determination of the duration of malaria infection, especially of fresh infections but excluding reinfections and relapses. This problem has been investigated by a team working in different parts of the U.S.S.R., as well as by unattached observers. The results obtained by the team (Rashina, 1941; Yakusheva, 1941; Dukhanina, 1941; Sheinker, 1941; Khovanskaia, 1941; Fastovskaia, 1941) were based on prolonged (2–3 years) epidemiological mass observations, analysed and treated statistically. These observations, extending from Arkhangelsk, in the North, to the Caucasus, in the South, have demonstrated that the duration of B.T. and M.T. infections was the same in different latitudes. It was found that in the majority of cases (90–95 per cent.) infection with *P. falciparum* disappears in the course of one year, while that with *P. vivax* may last 1½ years. The duration of infection did not exceed these periods even under conditions when there was considerable risk of reinfection. A certain number of cases become symptomless carriers (latent infections) 3–4 months after the attacks have ceased. In this connexion attention is drawn to the necessity of repeated examinations of the blood in persons with a history of recent malaria, and especially to the importance of dealing with carriers of M.T. in the spring months. It was demonstrated that prolonged treatment led to a considerable diminution of relapses.

It is concluded from these observations that, in the absence of acute manifestations of malaria in the course of one year, any attacks occurring in individual cases should be regarded as reinfections.

POLUMORDVINOV (1941) maintains that in Central Asia all acute cases of M.T. observed in the second half of the year should be attributed to fresh infections of the current year. Such cases terminate in May or June of the following year, the duration of the infection thus not exceeding 10–11 months.

FARAFONTOVA (1941) who followed up 472 cases of malaria in Rostov-on-Don, states that the duration of B.T. infections did not exceed two years, and that of M.T. one year, while the data for quartan malaria were insufficient to warrant any conclusions. Mixed infections —in various combinations—did not last more than two years.

NIKOLAEV (1941) deals with the duration of induced B.T. malaria, transmitted by mosquito bites. Observations on three cases showed that the maximum duration was about 2½ years.

LEVIN (1941) criticizes Schilling's method of studying the leucocyte changes in children during malaria which, he says, cannot be applied either to the control of treatment or for prognosis. According to this author, the "leucocytic profile" [=the plotting of leucocyte counts on curves] alone gives an exact picture of the leucocyte changes in children. It was found that, on admission, the majority of malarial patients exhibited neutropenia, half of them showed monopenia, and a few eosinopenia and lymphopenia.

Treatment and Drug Prophylaxis.

Therapeutic and prophylactic treatment with drugs forms the subject matter of the majority of papers under consideration. In describing the action of anti-malarial drugs the Russians employ a terminology which differs somewhat from that used in other countries. Thus, the action of drugs upon schizonts or gametocytes in general is described as *schizotropic* and *gamotropic* respectively. The effect of a gamotropic drug is said to be (1) *gametocidal* when it destroys the sexual forms, with the result that they disappear from the blood, or (2) *gamostatic*, when it inhibits the development of the gametocytes which, though still present in the blood, are rendered incapable of infecting the mosquito.

TIBURSKAIA (1941) compares the results of treatment of induced B.T. malaria with various combinations of Russian drugs. She found that daily administration of three tablets, each containing 0·1 gm. acriquine [=atebrin]+0·02 plasmocide [=Fourneau 710], prevented the infection of mosquitoes, the gamostatic effect being evident even 24 hours after the initial dose. However, plasmocide alone (0·06 gm. per diem) only lowers the infectivity to one-third. On the other hand, administration of pure quinoline No. 31 (0·06 gm. per diem) had a complete gamostatic effect in eight out of nine cases, but when combined with acriquine, its effectiveness was reduced, since about 50 per cent. of the mosquitoes became infected. It is concluded (1) that the effect of chemotherapeutic preparations, when administered jointly, does not represent merely the sum of their individual effects, but that there is some interaction between the constituent drugs, on the one hand, and between these and the host-tissues, on the other; (2) that combined treatment with acriquine and plasmocide should start as early as possible. It is noted that in combination with acriquine plasmocide loses much of its toxicity, a fact which was also established by LEVIT (1941) in tests on sparrows and mice.

SOLODOVNIKOVA (1941) describes the results of tests on the gamotropic properties of quinoline No. 31 in M.T. malaria, when given in doses of 0·03 and 0·06 gm. per diem. The results were checked by feeding *Anopheles maculipennis* var. *sacharovi* on treated patients. It was found that a single dose of 0·03 gm. had a very slight gamostatic effect after 24 hours, but two doses administered daily for five days had a considerable gamostatic and gametocidal effect. The latter dosage is, accordingly, recommended for prophylactic purposes.

One of the effects of gamotropic drugs being the inhibition of exflagellation of microgametocytes, SYRKINA (1941) has devised a method for observing this phenomenon in stained preparations. Blood from an infected bird is mixed with an equal amount of 3·8 per cent. citrate in an agglutination tube (about 0·5 cc. citrate to 10 drops of blood). The mixture is centrifuged for 15 minutes at 1,500 revolutions, after which thick films are made from the lower layer of plasma, while thin films are made from the upper layer of the deposit. The films are fixed in osmic acid vapour or 96 per cent. alcohol and stained by Giemsa's method. When present, microgametes ("free flagella") will be found in the thick films and these together with exflagellating gametocytes in the thin films.

MALYSHEVA (1940) reports the results of therapeutic and prophylactic treatment, with acriquine and plasmocide, of the population of 2,050 in a village in the Kabarda-Balkar republic (Caucasus) where M.T. is the prevalent form of malaria. No anti-mosquito measures were undertaken but treatment alone brought a diminution in the number of acute cases, though it failed to prevent the appearance of fresh infections. It is concluded that, in the presence of a high degree of transmission, drugs alone are incapable of eradicating the infection.

However, ARTEMENKO *et al.* (1941) are more optimistic. In certain parts of southern Ukraine, where they had been working, the chief foci of M.T. malaria are among the flood-banks of rivers where the vast areas involved preclude the adoption of anti-larval measures. The only practicable method of control in these localities is the detection and treatment of all cases. All parasite carriers were accordingly subjected to prolonged anti-relapse treatment with acriquine during the greater part of the vernal-aestival season. This was combined with prophylactic administration of plasmocide, lasting from the period when mosquitoes become infected to the period when they retire to hibernate. These measures have considerably reduced the incidence of malaria and the number of infected mosquitoes, and it is claimed that they may eventually lead to the liquidation of the foci of the disease in the country.

GALUSHKINA *et al.* (1941) were faced with the same problem on the Dnieper flood-banks. As a preliminary test they carried out prophylactic and therapeutic treatment with acriquine in two villages, in the course of two years. The treatment resulted in a marked diminution of the incidence of malaria. The authors maintain that, to be fully effective, treatment should be continued for several years. Prophylactic treatment can be restricted to early spring and the second half of summer (August–September) for the same group of people, in order to prevent fresh infections during the most dangerous period of the year.

In view of the increased incidence of B.T. malaria during the aestivo-autumnal period in the northern and central regions of Russia, LEVENSON (1940) recommends the introduction of chemoprophylactic

treatment in spring, during the pre-epidemic period. Since it is impossible to detect cases with a prolonged incubation period, the author advocates that priority of treatment should be given to the inhabitants of those districts and houses where the incidence of malaria was highest in the preceding autumn.

From experience gained in the Adjar Republic [Caucasus] AVALISHVILI (1940) states that, although prophylactic treatment with acriquine during the inter-epidemic period does not protect against fresh infections or relapses, it reduces their numbers, and is therefore to be recommended. Preference is given to interrupted treatment (0·2 gm. every third day).

ANDREIEV (1940), working in Kazakhstan [Central Asia], confirms the mitigating effect of prophylactic acriquine and suggests that it should be repeated in the course of several successive seasons, since treatment during one season is inadequate.

BARDOV (1940) reports successful results of prophylactic and anti-relapse treatment in an endemic malaria area occupied by peat-works in the Gorki province. With regard to the general incidence, the effect of chemoprophylaxis was more pronounced than that of anti-relapse treatment in the spring. In both forms of treatment acriquine produced better results than quinine.

KRANZFELD (1940) employed prophylactic treatment with acriquine among the Volga navvies who, on account of their work and mode of living, are particularly exposed to infection. Observations carried out in the course of one year, on 300 persons, showed that the incidence of malaria in those who had been treated fell to 8·9 per cent., as compared with 26·2 per cent. in control groups.

Working in the Middle Volga region, where both B.T. and M.T. forms of malaria are endemic, POLUMORDVINOV (1940) compared the results of two methods of chemoprophylaxis, in the absence of mosquito control. In one, 0·3 gm. acriquine was given on two consecutive days followed by an interval of eight days; in the other, 0·2 gm. acriquine+0·04 gm. plasmocide were given on two consecutive days with an interval of four days. The results of both methods were alike: they reduced the incidence of infection by half.

KHOVANSKAIA (1940) reports the results of prophylactic treatment in an estate of Tambov province (population 684), with a high incidence of M.T. and B.T. malaria (over 60 per cent.). Acriquine administered in doses of 0·2 gm. on three consecutive days followed by an interval of seven days proved to be ineffective, in the absence of anti-mosquito measures.

SAFRONOV (1942) obtained good results with prophylactic treatment of a community in the Transbaikal region, using acriquine in doses of 0·1 gm. twice a day, followed by intervals of four days. There was a considerable fall in case-incidence as compared with a neighbouring community not dealt with.

Control.

NABOKOV and ZAVYALOV (1942) discuss the conditions obtained in barrage-lakes covering a large area and comprising numerous bays, etc., which favour mosquito breeding. It is pointed out that the changeable character of such water collections (fluctuation in water level, amount of vegetation, and so forth) and the presence of various obstacles (such as tree stumps) may interfere with anti-larval measures.

It is suggested that more care should be taken in the early operations in order to ensure more adequate control of all parts of the system.

MIKHAILOV (1942) notes that the hydrotechnical measures undertaken since 1934 in Mariupol, on the Sea of Azov coast, and comprising the drainage and filling-in of anophelogenous swamps, have resulted in a marked diminution of malaria incidence, *viz.*, from 2,626 cases in 1935 to 390 in 1939.

SABANEYEV and SMIRNOV (1942) deal with hydrotechnical work in the flood-plain of the river Samarka, which aimed mainly at the reduction of the surface of water collections by filling-in, by drainage, and by connecting them by canals emptying into the river.

From experience obtained in the Ukraine, OVCHINNIKOV and TISHTENKO (1940) recommend periodical flushing of small rivers and canals for the destruction of anopheline larvae. The flush is controlled by dams or locks, the larvae being washed off and carried away by the current and then left dry on the banks when the water recedes.

LARIUKHIN (1942a) tested the larvicidal properties of oiled dust mixtures, consisting of 1 kgm. Paris green mixed with 19 kgm. talcum or road dust, with the addition of 2·2 to 3·8 per cent. masut or solar oil [=pyronaphtha]. The efficiency and the duration of toxic action of this composition upon anopheline larvae under field conditions were almost equivalent to those of unoiled preparations. In another paper this author (LARIUKHIN, 1942b) recommends a different larvicidal suspension which was successfully employed under field conditions. The proportions required per hectare are as follows: Paris green 0·8–1 kgm., kerosene 2·5–5 litres, and water 250 litres.

In an endeavour to utilize the local Altai products, SHESTERIKOVA and BUSHUROVA (1942) tested "light tar," a liquid by-product of the tar-turpentine industrial process, as well as certain plants. The tar proved to be highly larvicidal in quantities of 300 gm. per sq. metre but, since it is lethal to aquatic plants and animals, it can be applied only to water collections of no economic importance. Among plants, powdered *Pyrethrum* sp. and *Cicuta virosa* appeared to be promising, whereas *Thermopsis lanceolata* and *Hyoscyamus niger* had no larvicidal effect.

GRECHKA and BIELSKAYA (1942) have employed with success a larvicide made with an arsenical ooze obtained as a by-product from chemical works. This substance (containing 10·6 per cent. arsenic trioxide and 7·8 per cent. arsenic pentoxide), when dried and powdered, can be mixed with a threefold amount of dust and used in doses of 3 kgm. per hectare for ordinary dusting, or it can be mixed with 2 per cent. petroleum for spraying from aeroplanes, in doses from 1 to 2 kgm. per hectare.

SHIMANSKY (1942) describes a new pneumatic sprinkler for liquid larvicides, which can be used from a boat or cart.

Working in the Ukraine, in large anophelogenous areas, overgrown with vegetation and unsuitable for drainage or dusting, NIKULIN (1941) believes that in such localities it is more practicable to control the adult mosquitoes than the aquatic stages. This is done by catching them daily in the dwellings.

LAZEBNY (1941) describes the successful application of this method in two settlements in the Crimea. In this campaign the local population—mainly housewives—took a prominent part, thus releasing professional "bonificators" for more important duties. The women were trained to detect and destroy the mosquitoes in their homes, in the

course of their daily domestic duties. These measures brought about a considerable reduction in the number of mosquitoes in the dwellings (as shown by comparison with a control house) and resulted in a fall in the incidence of malaria in the localities in question.

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An extensive review, appearing in the journal under consideration, is devoted to an important publication by STACKELBERG (1940), *Bibliography of Malaria,* which deals with the literature on the epidemiology, parasitology, transmission and prophylaxis of malaria in U.S.S.R., the references being not only to Russian, but also to foreign work. This monumental volume, covering the literature of the last 165 years and comprising 7,053 references, will form a unique and valuable addition to medical bibliography. It is not clear whether this publication can be readily obtained, for although its price (95 Roubles) is marked, it is said to be " For official use."

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SUMMARY OF RECENT ABSTRACTS.*

IV. TRYPANOSOMIASIS.

Aetiology : Transmission.

ZSCHUCKE (p. 605) has examined strains of *T. gambiense* from the island of Fernando Po, where the disease has been known for over a century. In 1929 he failed to find posterior-nuclear forms in infected

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1942, Vol. 39. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

mice and guineapigs, but 10 years later he repeated this work, and saw these forms in 6 of 10 strains investigated, though in very small numbers. In mice they were only present after intracerebral inoculation, or after intravenous inoculation in animals which had received intracerebral injection of 2 per cent. starch solution. He concludes that the trypanosome has become more virulent in the last 10 years, and relates this to the continued introduction of susceptible natives into the island. These facts furnish additional evidence of the identity of *T. gambiense* and *T. rhodesiense*.

ROUBAUD and PROVOST (p. 234) trace the course of infection in mice with a strain of *T. gambiense* which shows great irregularity in its pathogenic effects in those animals. This infection may follow the normal course, with numerous trypanosomes in the blood, or it may be neurotropic, leading to posterior paralysis. In this case the blood usually contains few trypanosomes, but an emulsion of the brain may be infective.

JACK (pp. 443, 817) has continued his observations of *G. morsitans* in the Zambesi valley, where in the hot season the shade temperature may reach 106°F. and where the wild flies may lose water in excess of replacement. In many localities, cooler refuges than those afforded by simple shade are essential for *G. morsitans* during the latter half of the dry season, and in especially hot periods the fly might suffer a severe setback. In certain kinds of riverine forest, however, the evaporation rate is much lower than standard meteorological records indicate. The author gives in detail his findings on the fat and water content of flies examined in relation to feeding, site and other factors.

In Northern Nigeria *G. morsitans* and *G. tachinoides* annually in March shift their breeding ground from the edge to the centre of a residual forest island—a distance of 40 yards. NASH (p. 532) attributes this move to a negative reaction to light when the flies are exposed to high temperatures.

NASH (p. 234) points out that in Nigeria bats may be an important source of food for *G. tachinoides* and *G. morsitans* when floods force the game away from the tsetse-infested river plain.

Pathology: Clinical Findings: Treatment.

HAWKING and GREENFIELD (p. 235) describe the post-mortem findings in two cases of *T. rhodesiense* infection, in which no effective treatment had been given. In each case there were tuberculous foci in lungs, liver, spleen and glands. Trypanosomes were present in the blood and in effusions found in the pleura, pericardium and peritoneum, and there was subacute inflammation of the myocardium and epicardium. The cerebrospinal fluid contained numerous trypanosomes but the changes in the central nervous system were limited to histiocytic infiltration of the cerebral membranes. It is concluded that, in the absence of treatment, the visceral lesions of *T. rhodesiense* infections are probably more often fatal than the lesions of the nervous system.

VAN ZYL and GEAR (p. 236) describe the course of trypanosomiasis in a European who refused all treatment. The infection was acquired in N. Bechuanaland and proved fatal within six months; it was probably due to *T. rhodesiense*. A brother of this patient was infected at the same time but was apparently cured by a course of Bayer 205.

As a result of work on animals infected with *T. brucei*, VAN DEN BRANDEN (p. 237) considers that a complement-fixation reaction may

be applied in the diagnosis of human trypanosomiasis, or as an estimate of prognosis during the course of treatment. The serum of rabbits gives positive results with an antigen of *T. brucei* if the animals have had the infection for a considerable length of time, but the test becomes negative after treatment. There is, however, the difficulty of obtaining a suitable antigen, since the blood of laboratory animals infected with *T. gambiense* is not sufficiently rich in parasites for the purpose.

HAWKING and SMILES (p. 238) have used the property of fluorescence, possessed by 4 : 4′ diamidino-stilbene, to study its distribution in trypanosomes and in the bodies of animals. It is absorbed in large quantities by trypanosomes and is deposited in the blepharoplast and in granules in the cytoplasm. In mice it is found in the liver and kidneys, and possibly in the small intestine and skin ; it is excreted in the urine (markedly within seven hours, ceasing within two days) but probably not in the bile.

MAYER (p. 239) discusses the selective action of drugs on definite constituents of trypanosomes, for instance the effect of Bayer 205 in preventing division of the cytoplasm in spite of the fact that nucleus and blepharoplast may divide. Finally, there may be produced forms without blepharoplast or nucleus. Antimonials act on the nucleus ; the action of synthalin resembles that of Bayer 205, but Mayer gives evidence to suggest that it acts primarily on the blepharoplast.

As a result of prolonged observation of patients with *T. gambiense* infection, treated with Bayer 205, SAUNDERS (p. 534) has reached the conclusion that even in advanced cases this treatment may produce remission lasting for many years.

KUNERT (p. 818) has shown that Bayer 205, when given in doses of 3 gm. intravenously or by the mouth, reaches the cerebrospinal fluid, but in only ½ to ¼ the concentration present in the serum. Treatment of late stages of *T. rhodesiense* infection with Bayer 205 is often unsuccessful even if three doses, each of 3 gm., are given at five-day intervals, since, although there is a temporary action on the trypanosomes, relapse in the cerebrospinal fluid occurs, probably owing to the presence of drug-resistant trypanosomes. The trypanosomes probably reach the cerebrospinal fluid from the tissue of the choroid plexus.

HUMPHREYS and DONALDSON (p. 240) have found that, in toxic doses, Bayer 205 consistently produces zonal degeneration of the adrenal cortex of small laboratory animals, but there is evidence to suggest that healing may take place relatively quickly if the injections are stopped. Spacing of the doses is important ; animals injected on alternate days showed a much greater death rate than those injected at intervals of eight days. It is noted that doses comparable to those used therapeutically in man may produce similar but less intense adrenal cortical lesions in animals.

HAWKING (p. 534) has tested the toxicity of Bayer 205 for mice ; the work cannot be further summarized.

FULTON and YORKE (p. 533) note that an atoxyl-fast strain of *T. rhodesiense* has preserved its character for 12½ years, and that other strains, resistant to Bayer 205 or undecane-diamidine, have lost part of their resistance after periods up to four years.

SAUNDERS (p. 532) has treated 14 cases of sleeping sickness in the Gold Coast with 4 : 4′ diamidino diphenoxy pentane (pentamidine). He reports that early cases appear to be cured and that untoward effects are trivial.

In work on cattle infected with *T. congolense*, DAUBNEY and HUDSON (p. 533) found that pentamidine in doses of 10 mgm. per kilo. produced immediate poisoning with collapse and death, and that delayed poisoning was caused by repeated injections of 5 mgm. per kilo. Descriptions of the effects of delayed poisoning are given.

FRIEDHEIM (p. 444) records his experience with the substance known as azo-arseno-benzol 4197, which contains 13·8 per cent. of arsenic. He has used this compound for the treatment of trypanosomiasis and syphilis in French West Africa, the standard dose for an adult being 0·5 gm. given intravenously in 5 per cent. watery solution, and repeated 8–12 times at intervals of 2–4 days. The immediate results of this treatment, in a small number of cases, some of which had proved resistant to previous treatment, were favourable. This compound, unlike other arsenobenzols, can traverse animal membranes, and can be found, in animals, in the aqueous humour and the cerebrospinal fluid after intravenous injection.

Control.

In the Cameroons, when sleeping sickness was at its height from 1922 to 1929, classification was made into three types of zone :—Epidemic, with an infection rate of over 15 per cent., Endemo-epidemic, with rates round 15 per cent., and Endemic or Transition, with lower rates. VAUCEL (p. 743) refers to the work of the prophylactic missions in the Cameroons and demonstrates the great improvement which has taken place in recent years, largely through the wide use of chemotherapy. He points out, however, that chemotherapy alone does not completely eradicate the disease.

In his report on the Belgian Congo for the year 1940, VAN HOOF (p. 815) notes that the index of new infections has decreased, but that the frequency of drug resistant cases has increased. Certain foci have persisted despite all efforts ; in such areas control with Belganyl (Bayer 205) leads to great, but not complete, reduction in the endemic index. He gives some details from the various provinces, noting in particular that the constant movement of fishermen on the lakes favours the spread of sleeping sickness and other diseases. He suggests the prophylactic use of Bayer 205 in fishermen.

GIBBINS (p. 442) describes the principles of "rod clearing," as applied to the rivers and streams of the West Nile district of Uganda for the control of sleeping sickness transmitted by *Glossina palpalis*. This fly is confined to the immediate vicinity of rivers and streams, and the clearing of bush from the banks to a depth of 10 yards, for distances of not less than 800 yards, is enough to protect villages or crossings situated in the middle of the clearings. Grass must, however, be kept short ; tall grass is even more attractive to the fly than untouched forest. Tall trees may be left if their branches are cut away to a height of 15 feet. It is not clear what factors limit the flies to water, humidity is not a factor. The effectiveness of the rod clearings is possibly due to their preventing the flies from lingering near the water where they would be exposed to the large numbers of predacious dragon flies which constantly patrol the sunlit stretches.

STAPLES (p. 606) considers that it is incorrect to consider that the clearing of bush in Tanganyika Territory, as an anti-tsetse measure, encourages soil erosion. He claims, on the contrary, that it decreases

erosion in these semi-arid conditions where the ground vegetation is thin, and that it is probably essential to the full use of land for mixed farming.

MALBRANT (p. 242) does not accept the view that the destruction of game is useful as a measure of control of trypanosomiasis, since, if deprived of game, the flies would be maintained on birds, reptiles, rodents and other animals not classed as game, and they would be driven to rely more on man and domestic animals than they now do. It is known that the distribution of game and tsetse flies does not invariably correspond, and even in the case of *G. morsitans* the close correspondence of distribution with that of game may be due rather to the fact that conditions are favourable both to flies and game than to any preference of flies for game. Moreover, the author claims that there is no proof that big game can be a reservoir of *T. gambiense*, and that the ease with which infections with *T. rhodesiense* can be eradicated from human communities, by proper treatment, without any change in the animal population, shows that game plays little part in the conservation and propagation of this trypanosome.

HORNBY (p. 242) traces the history of a small herd of cattle, some inoculated with killed *T. brucei* and *T. congolense*, some given minimal infections, and some controls. The animals lived out their lives in areas in which natural infection was possible, though for a time not heavy, and after about seven years practically all were dead of trypanosomiasis. SCHILLING, who had initiated the experiment, had considered that there was a possibility that protection might be offered by the inoculations and the minimal infections, but Hornby concludes that there is nothing in the whole experiment to furnish hope that any practical method of immunization is in sight.

CHAGAS'S DISEASE.

ROSENFELD & CARDOSO (p. 247) give an account of the incidence and the vectors in the State of São Paulo. Infected *Triatoma infestans* and infected dogs have been found by CARDOSA and NAVAJAS (p. 248) in the State of São Paulo, but no cases of human disease were seen. VON BÜLOW (p. 606) reports Chagas's disease, for the first time, in Costa Rica ; the local vector is *Triatoma dimidiata*. OTÁLORA (p. 820) reports the first cases from Colombia. TALICE *et al.* (p. 536) note that half of the *Triatoma infestans* found in dwellings in a district of Uruguay were harbouring *Trypanosoma cruzi*. A number of infected persons were found, but there were no cases of acute disease. Symptoms included loss of weight, adenitis, anaemia and monocytosis. TORREALBA and RICCARDI (pp. 245, 248) report a few human cases in Zaraza, Venezuela. PIFANO (p. 245) gives an account of Chagas's disease in part of Venezuela. The most important vector was *Panstrongylus geniculatus*, and 10 species of animals were found to be naturally infected, including the armadillo, opossum, cat, dog and rat. Cases of Chagas's disease are recorded from the Province of Corrientes, Argentina (TORANZOS *et al.* p. 244). GASIC and BERTÍN (p. 246) give an account of the disease in Chile, where a high proportion of *Triatoma infestans* has been found infected, and where dogs and cats are among the naturally infected animals.

DARMAN (p. 745), in attempting to enhance the virulence of two strains of *T. cruzi* by passage through mice, found that virulence was not related to the number of flagellates in the peripheral blood, but

remained a function of the individual strain, and was greatly different in the two strains investigated. Cross immunity tests emphasized the difference between the two strains.

MAZZOTTI and LEON (p. 671) quote evidence to show that *T. carrioni* is a probable vector in part of Ecuador and that the disease is probably endemic there. PIFANO (p. 247) reports that he has found *Amblyomma longirostrum*, a parasite of the porcupine, naturally infected with *T. cruzi*. MAZZOTTI (p. 247) has shown that the Cimicid bug, *Haematosiphon inodorus*, can be infected with *T. cruzi* by feeding upon infected mice, and that metacyclic forms of the trypanosome can be found in the faeces some 15 days after feeding. At that time the intestinal contents of the bug are infective to mice. WOOD (p. 244) has found Triatoma, infected with *Trypanosoma cruzi*, in five areas of Texas from which infection has not hitherto been reported. Two bugs, *T. longipes* and *T. protracta woodi*, have for the first time been found naturally infected. In these areas the relationship between man and bugs is intimate, and the strains of *T. cruzi* are virulent. He advises that unilateral palpebral oedema in man in infected areas should be viewed with suspicion as probable evidence of Chagas's disease.

WOOD (p. 445) gives a list of the Triatomids collected in the south-western United States. Species found infected with *T. cruzi* were *Triatoma protracta*, *T. protracta woodi*, *T. rubida*, *T. longipes* and *T. gerstaeckeri*. He (p. 671) allowed a number of non-infected Reduviid bugs to feed on his arm, with the object of determining what after-effects occurred. Late local reaction was produced by one only of the eight species tested. The experiments were undertaken to draw a distinction between the effects of the bites of non-infected and infected bugs, since a prevalent symptom of infection is palpebral oedema.

TORRES (p. 672) has found, in infected puppies, cellular infiltration round the myocardial capillaries, and damage to the endothelium. The infiltration is held to be due directly to the capillary damage, and is not associated with the presence of trypanosomes; the latter are found agglomerated in tissues between the muscle fibres.

MAZZA *et al.* (p. 446) draw attention to the intermittent fever which is associated with the presence of *T. cruzi* in the blood, and point out that a fairly constant feature in some cases is a double peak in the 24 hours. This form of chart is found to coexist with the leishmanial forms of the parasite invading the tissues, and brings the disease more into line with kala azar. In comment, SCOTT points out that kala azar exists in the Argentine, where Mazza's cases were seen, and that in such cases it would be well to exclude coexistent kala azar as a cause of the peculiar temperature curve, since hitherto the double peak has been regarded as an indication of kala azar.

MAZZA *et al.* (p. 671) record a number of cases of meningo-encephalitis in Chagas's disease. In some instances this complication appeared early, in others late, but at any time it is serious. The only effective treatment is stated to be the intramuscular injection of Bayer 7602 in doses of 100 mgm. per kilo., given repeatedly.

MAZZA and SALICA (p. 248) describe three types of chagoma:—(1) Chagoma of inoculation, a swelling at the site of original inoculation. (2) Metastatic chagomata, satellites of the primary chagoma. (3) Haematogenous chagomata, multiple and probably blood-borne, appearing at a distance. They describe the histology, in which inflammation of the skin and cytosteatonecrosis of the subcutaneous tissues are features; leishmanial forms of *T. cruzi* are demonstrable in the histiocytes.

MAZZA *et al.* (p. 249) describe a patient with a primary chagoma of the neck, and a general erythematous eruption. Leishmanial forms of the trypanosome were found in a biopsy specimen taken from a site where the rash was prominent.

Discussing the diagnosis of Chagas's disease, TORREALBA (p. 746) states that the value of the Machado reaction is debatable, the examination of thick blood films is likely to be positive in early cases only, and blood inoculation is not successful. He considers, therefore, that xenodiagnosis is the method of choice, and for this purpose he uses *Rhodnius prolixus* or *Eutriatoma maculata.*

MAZZA (p. 820) gives the history of the drug known as Bayer 7602, which has proved valuable in the treatment of Chagas's disease in the acute stages. Intramuscular injections, in doses of 30–120 mgm. per kilo. body weight, are given without rest periods unless albuminuria is produced, and it has been found that trypanosomes disappear from the blood. PIFANO (p. 245), however, notes that although some of the clinical signs of the disease appeared to recede after the fifth dose of Bayer 7602, he has observed like results in patients who received no treatment.

SINJOVICH and SOMAINI (p. 246) report apparent cure in one case in which treatment included the use of paroxyl (0·02 gm. per kilo. body weight) and dicalose and arrhenal 0·1 gm. daily. *Charles Wilcocks.*

MALARIA.

SCHWETZ (J.), with the collaboration of H. BAUMANN, Mme. BEUMER & M. FORT. Sur le paludisme endémique dans la vallée de la Semliki et sur les rives du Lac Albert. [**Endemic Malaria in the Semliki Valley and on the Shores of Lake Albert.**]—*Ann. Soc. Belge de Méd. Trop.* 1941. Dec. 31. Vol. 21. No. 4. pp. 339–373. With 1 map.

Four days spent in the Semliki Valley, south-east of Beni, and 11 days on the shore of Lake Albert, in and around Kasenyi, enabled the author to obtain blood smears from 1,067 natives, and his trained entomological assistants to make collections of adult and larval Anopheles in these relatively low-lying situations and on adjacent plateaux. The River Semliki here is about 800 metres above sea-level. The subsequent examination of this material is the basis of this very detailed preliminary report.

In the Semliki valley the two most common of the Congo malaria vectors, *A. gambiae* and *A. funestus*, both occur. Endemic malaria was found in all the six villages in the valley that were visited. The endemicity varied a little from place to place but was not intense. Parasites were rarely numerous; *P. vivax* was not found, and *P. malariae*, frequent in the children, was not once found infecting adults. A village on a plateau about 1,800 metres high was free from malaria.

In and around Kasenyi on the south-west shore of Lake Albert, *A. gambiae* was rarely found. *A. funestus* and *A. pharoensis* were much

more prevalent ; they are the dominant anophelines in Kasenyi. The parasite rates were high among children, but in the vast majority of positive films the parasites were excessively rare. The degree of endemicity was lower than the relatively intense anopheline infestation had led the author to expect. The age distribution of *P. malariae* infections followed the general rule. Some *P. vivax* infections were found in young children. It is curious that nearly all the gametocytes found were of *P. malariae*. Crescents were very rarely seen. It is also surprising that two villages on neighbouring plateaux some 1,450 metres high, in which anophelism was much less intense than on the lake shore, appear to have a degree of malaria endemicity almost if not quite as high as that of Kasenyi and its neighbourhood.

Norman White.

BLACKLOCK (D. B.) & WILSON (Carmichael). **A Late Seasonal Increase of *Anopheles funestus* in Village Houses.**—*Ann. Trop. Med. & Parasit.* 1942. Dec. 31. Vol. 36. No. 4. pp. 182–186. With 2 figs. on 1 plate.

The observations reported in this paper were made in a West African village in the houses of which *A. gambiae* greatly outnumbered *A. funestus* from April to July, whereas from September to December *A. funestus* was much the more prevalent species. *A. gambiae* was breeding in rock-pools, earth-pools, street-drains, in the streets and compounds of the village, and in pools in potato and sugar-cane farms. *A. funestus* bred in springs well concealed by long grass and shrubs, which were only discovered by systematic search. Most of these springs are seasonal ; they function as such only after the rains have persisted for some time and caused sufficient rise in the ground water. Thus is explained the late seasonal increase in *A. funestus* density. A full year's study of local conditions is a necessary prelude to undertaking permanent measures to eliminate breeding in springs, in places such as this.

Norman White.

BLACKLOCK (D. B.) & WILSON (Carmichael). **Simple Anti-Malaria Methods for Use in Villages.**—*Ann. Trop. Med. & Parasit.* 1942. Dec. 31. Vol. 36. No. 4. pp. 187–191. With 6 figs. on 3 plates.

The villages considered in this paper are constructed on sloping ground on laterite rock with but a shallow covering of earth. Efforts at increasing and improving the agricultural output of such villages appear to have resulted in increased malaria incidence. The methods of agriculture in the small compound farms have provided increased facilities for *A. gambiae* breeding. It is common for all available earth to be heaped up into mounds on which cassava and other crops are grown, the rock between the heaps being left bare. This exposed rock provides numerous breeding places for *A. gambiae*. If the earth be not thus heaped the layer of water on the rock surface beneath the thin layer of earth causes the plants to rot.

The authors describe methods they have used to get over these difficulties. Terraces have been made ; stones and pebbles on the rock surface form a filter bed on which the soil is replaced. Additional soil and sufficient composted material are often required. Improved agricultural output and much lessened *A. gambiae* prevalence can thus be obtained.

Norman White.

BRUMPT (E.) & DAO VAN TY. Distribution des biotypes d'*Anopheles maculipennis* en France. [**Distribution of the Varieties of** *A. maculipennis* **in France.**]—*Ann. Parasit. Humaine et Comparée.* 1942. Vol. 19. No. 1–2–3. pp. 69–73.

BANG (Frederik) & SIMPSON (Thomas). **Feeding Habits of** *Anopheles walkeri* **Theobald at Reelfoot Lake, Tennessee.**—*Amer. Jl. Trop. Med.* 1942. Sept. Vol. 22. No. 5. pp. 513–516. [13 refs.]

It is known that *Anopheles walkeri* can be infected experimentally with malaria parasites, that it has been found infected in nature, and that in some areas it is the prevalent anopheline. By precipitin tests the authors have found human blood in 9 of 105 *A. walkeri* caught in cowsheds and other places. Experiments showed that when man was as available as domestic animals to the mosquitoes, attraction to man was about equal to that shown towards animals. *C. W.*

KUMM (Henry W.). *Anopheles crucians* **found in Northern Nicaragua.** —*Amer. Jl. Trop. Med.* 1942. Sept. Vol. 22. No. 5. pp. 511–512. With 1 fig. (map).

The author reports the finding of *A. crucians* in N. Nicaragua, further south than was previously known. Other anophelines seen were *A. albimanus A. argyritarsis*, *A. strodei* and *A. punctimacula.* *C. W.*

SEN GUPTA (P. C.). **Urticaria due to Malarial Infection.**—*Indian Med. Gaz.* 1942. July. Vol. 77. No. 7. p. 416.

" A case where every paroxysm of malarial fever was accompanied by urticaria is reported. This is probably an instance of a very rare condition—hypersensitiveness to malarial parasites, producing urticaria."

SCHOENBACH (Emanuel B.) & SPINGARN (Clifford L.). **Inoculation Malaria and Drug Addiction.**—*Jl. Mt. Sinai Hosp. New York.* 1942. Jan.–Feb. Vol. 8. No. 5. pp. 998–1004. [23 refs.]

The authors report two cases of malaria in drug addicts in which infection had been acquired by the intravenous injection of heroin by means of primitive apparatus shared by a number of addicts without any attempt at disinfection or cleansing of any kind before or after use. A very large number of similar cases have been reported in the literature and most of them have certain features in common. Very primitive apparatus is used for making the injections, in these cases an eye-dropper with a rubber nipple and a hypodermic needle. The drug used by most of these addicts suffering from malaria has been heroin. It is probably the most common drug of addiction, but heroin addicts, unlike morphine addicts, are extroverts seeking the companionship of other victims of the drug. Thus the use of a common syringe is most likely in this form of addiction. The symptoms in these cases are rarely typical of malaria. " The presence of signs of venipuncture, thrombosed basilic veins, and irregular fever should lead one to suspect strongly narcotism and malaria." The authors refer to many of the very large number of reports of similar cases that

have been published ; the bibliography contains 23 references. [See also this *Bulletin*, 1941, Vol. 38, pp. 106, 174, 175, 644. Further references are given in these abstracts.] *Norman White.*

i. HEILIG (Robert) & VISWESWAR. **Quinine Diuresis in Malarial Conditions.**—*Indian Med. Gaz.* 1942. Sept. Vol. 77. No. 9. pp. 513–517.

ii. INDIAN MEDICAL GAZETTE. 1942. Sept. Vol. 77. No. 9. pp. 545–546. With 1 graph.—**The Kidney in Malaria.**

i. Heilig & Visweswar describe two cases in which the administration of quinine was followed by the disappearance of ascites and general anasarca which had failed to respond to the usual diuretic remedies. The first case was that of a boy of 5 years who was admitted to hospital suffering from generalized oedema and a very large ascites. He had suffered from attacks of fever during the previous six months. No malaria parasites were found in the blood but the malaria flocculation test gave a positive result. The Wassermann and Kahn reactions were negative. The scanty urine contained much albumin, red blood cells, leucocytes, and hyaline and granular casts. Two weeks of energetic treatment with the usual diuretics gave no relief ; the general condition became much worse. Then fifteen grains of quinine a day were given ; this was later reinforced with a daily intramuscular quinarsol injection. After 16 days of this treatment the ascites and oedema had completely disappeared and the body weight was reduced from 41 to 25½ pounds. The clinical improvement was fully maintained during the four weeks after the cessation of the quinine treatment, and a persistent albuminuria was the sole remaining pathological sign.

The second patient, a coolie aged 28, was admitted to hospital in a similar water-logged condition. He too gave a history of recent attacks of malaria but no parasites were found. The malaria flocculation test was positive, the Kahn and Wassermann reactions negative. There was only a trace of albumin in the scanty urine. Treatment with urea and ammonium chloride, and the elimination of 40 hookworms, reduced the weight of the patient by forty pounds and caused the disappearance of the oedema, but the large ascites persisted, almost unchanged, four weeks after admission. Daily intravenous injections of quinine were given for ten days ; ten grains of quinine a day was also given by mouth. The ascites disappeared completely. There was some reduction in size of the large spleen, and the haemoglobin content of the blood increased from 45 to 50 per cent. (Sahli) : it had been only 23 per cent. on admission.

In commenting on their cases the authors state that malarial nephritis reported in the literature has been almost exclusively connected with *P. malariae* infections. In their practice *P. malariae* is very rare, and when parasites have been found in such cases they have been P. *vivax*.

ii. In a leading article the *Indian Medical Gazette* reviews the literature of malarial nephritis. Regarding the mechanism of production of subacute glomerular nephrosis perhaps the most plausible suggestion is " that it is an allergic phenomenon due to previous sensitization of the kidney, in susceptible individuals, by ' foreign ' protein substances derived from parasite and host-tissue destruction resulting from the malaria infection and its cure." *Norman White.*

WEED (Lewis H.). **The Critical Antimalarial Problem and its Solution.** —*Jl. Amer. Med. Assoc.* 1942. Nov. 28. Vol. 120. No. 13. pp. 1043–1044.

The critical problem dealt with is that arising from the facts that the loss of Java deprived the allies of the source of 90 per cent. of the world's pre-war supply of quinine, and that military operations are taking place to a large and increasing extent in countries in which malaria is endemic or hyperendemic. To make the most of the limited stocks of quinine available, the National Research Council and the War Production Board of the United States framed the measures which are set out in this paper.

The use of quinine and other cinchona alkaloids is restricted to the treatment of malaria, except that quinidine may be used in the treatment of cardiac disorders, and quinine may be used in the treatment of myotonia congenita. Persuasive efforts have been made to collect all stocks of quinine in the United States.

More use is to be made of totaquine. Totaquine was recognized officially in the 12th edition of the U. S. Pharmacopoeia; it was considered, however, that the constitution of totaquine therein described allowed too much latitude. On the advice of the National Research Council the U. S. Pharmacopeia has now adopted the following definition: "Totaquine is a mixture of alkaloids from the bark of Cinchona succirubra Pavon and other suitable species of Cinchona. It contains not less than 7 per cent. and not more than 12 per cent. of anhydrous quinine, and a total of not less than 70 per cent. and not more than 80 per cent. of the anhydrous crystallizable cinchona alkaloids, the designation 'crystallizable alkaloids' referring to cinchonidine, cinchonine, quinidine and quinine." It is recommended that the dose be 10 grains three times a day for seven days.

The production of atebrin is sufficient to supply all anticipated needs. Pharmacological and clinical investigations have shown that a variable percentage of persons receiving atebrin as a clinical prophylactic have temporary gastrointestinal disturbances. The yellow pigmentation of the skin during administration is harmless and not associated with any disturbance in liver function.

The Subcommittee on Tropical Diseases of the National Research Council recommends as an efficient therapy routine:

(1) *Combined QAP Treatment* (method of choice):—

(*a*) Totaquine or quinine sulphate, 10 grains, thrice daily after food, for 2 or 3 days or till fever is controlled.

(*b*) Atebrin 0·1 gm. thrice daily after meals for the next five days.

(*c*) Two days without antimalaria medication.

(*d*) Plasmoquine 0·01 gm. thrice daily after meals for five days (twice daily for debilitated patients).

(2) *Atebrin-Plasmoquine Treatment*:—

In simple *P. vivax* infections, or when no quinine or totaquine is available, atebrin in the above doses may be given for 7 days, then two days free from antimalaria medication followed by five days plasmoquine medication as above.

(3) *Totaquine or Quinine-Plasmoquine Treatment*:—

If no atebrin be available give totaquine or quinine as above for seven days during the last five days of which associate each dose of totaquine or quinine with plasmoquine 0·01 gm. (thrice daily).

(4) *Suppressive Treatment* :—

Atebrin 0·1 gm. twice daily after food twice a week. Allow two or three days' interval between days of medication.

It is recommended that pending more experience atebrin should only be given under the guidance of a physician or public health officer.

Cinchona barks from South America with a low quinine content, but sufficiently rich in total crystallizable alkaloids to make totaquine, may be available in sufficient quantity to enable totaquine to replace civilian quinine requirements in the U.S.A.

[In this communication the only salt of quinine referred to is the sulphate, which is soluble in cold water to the extent of 1 in 800 only ; for use in solution it is necessary to add 1 minim of dilute sulphuric acid for each grain of the salt. Quinine bisulphate and quinine bihydrochloride are, of course, much more soluble. For a discussion of modern methods of treatment and prophylaxis of malaria see this *Bulletin*, 1942, Vol. 39, p. 801.] *Norman White.*

RUSSELL (Paul F.) & MENON (P. Balarama). **On the Transmission of *Plasmodium gallinaceum* to Mosquitoes.**—*Amer. Jl. Trop. Med.* 1942. Sept. Vol. 22. No. 5. pp. 559–563. With 3 figs.

In a previous paper [this *Bulletin*, 1943, Vol. 40, p. 17], RUSSELL and MOHAN reported the experimental infection of 12 species of mosquitoes of the genera Armigeres and Aëdes with *Plasmodium gallinaceum*. In the present paper five more species are added to the list and it is stated that there has never been failure with any species of these genera which have been tested. With species of Anopheles and Culex results have been very different, for there was development of some oöcysts in only a single specimen of *Culex mimuloides*. In contrast to the avidity with which *Aëdes albopictus* and *Armigeres obturbans* fed on all parts of the fowl, species of Culex and Anopheles were reluctant to feed even when feathers had been removed from an area on the back of the fowl. It would appear unlikely that local species of Culex and Anopheles are natural hosts of *P. gallinaceum* in Madras, where the observations were made. *C. M. Wenyon.*

RUSSELL (Paul F.) & MOHAN (B. N.). **The Immunization of Fowls against Mosquito-borne *Plasmodium gallinaceum* by Injections of Serum and of Inactivated Homologous Sporozoites.**—*Jl. Experim. Med.* 1942. Nov. 1. Vol. 76. No. 5. pp. 477–495. With 1 chart. [12 refs.]

The authors describe attempts to immunize fowls against *Plasmodium gallinaceum* infections by repeated injections of inactivated sporozoites or of serum from normal sheep or chronically infected fowls. When tested subsequently by feeding infected mosquitoes upon them, the groups of fowls which had been treated were found to have some degree of immunity as shown by the reduced death rate and by the lowering of the average maximum percentage of red cells infected during the course of the infection. When fowls were immunized by repeated injections of both vaccine (emulsion of dried thoraces of infected mosquitoes) and serum, a higher degree of immunity was attained, as proved by the lowering of the death rate from 55·4 per cent. in the controls to 7·3 per cent. in the treated fowls. The average highest

percentage of infected red cells in untreated fowls was 30·1 per cent. By the combined methods of immunization this figure was reduced to 15 per cent. It has been shown that the injections of normal sheep serum or that of chronically infected fowls will increase the size of the spleen to double its normal volume. It is concluded that the results appear to indicate an interaction of both cellular and humoral agencies in defence against malaria, since the greatest immunizing effect was produced by a combination of vaccine and serum injections.

C. M. Wenyon.

PURCHASE (Harvey S.). **Turkey Malaria.**—*Parasitology.* 1942. Nov. Vol. 34. Nos. 3/4. pp. 278–283.

A malarial parasite of turkeys was discovered in a number of birds from different localities in Kenya. The disease induced by artificial inoculation of infective blood is highly fatal to young poults. Schizonts are frequently found in endothelial cells of blood vessels. A prominent feature of the post-mortem appearance of birds which have died of the infection is the accumulation of pigment in the spleen, liver and mucous membrane of the duodenal loop. Pigment is present in smaller quantity in the lungs and kidneys. In the chick a transient infection can be produced but ducks and adult fowls seem to be refractory. The author states that he has been able to trace only one reference to malaria in turkeys, namely that of PARCVANIDZE in 1914. It is possible, however, that MACFIE's *Halteridium* sp. of the turkey in West Africa (1915) may be identical with the malarial parasite considered in the present paper, a complete description of which is to be given by Dr. Carlton HERMAN who studied the parasite when on a visit to Kenya. *C. M. Wenyon.*

BLACKWATER FEVER.

FOY (Henry), ALTMANN (Alfred), BARNES (H. D.) & KONDI (Athena). **Anuria. With Special Reference to Renal Failure in Blackwater Fever, Incompatible Transfusions, and Crush Injuries.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1943. Jan. 30. Vol. 36. No. 4. pp. 197–238. [213 refs.]

The purpose of this paper is to examine the present status of the problem of anuria and oliguria occurring in such syndromes as blackwater fever, favism, incompatible transfusion and crush injuries, and to suggest that the renal abnormalities occurring in all these diseases have a similar basis. The hypothesis that anuria occurring in the haemoglobinurias of incompatible transfusions, blackwater fever and in rabbits injected with haemoglobin solutions is the result of mechanical blockage of the renal tubules with haemoglobiniferous products, especially when the urine is acid, is insufficient to account for all the facts, and in the light of recent work seems an improbable explanation. The view that oliguria and anuria can be prevented by the simple process of "alkalizing" the urine is not borne out in the majority of cases and on physiological grounds seems unlikely.

After briefly summarizing the earlier observations of PLEHN (1903), PONFICK (1883), WERNER (1907) and DE HAAN (1905), and particularly

those of BARRATT and YORKE (1909) and YORKE and NAUSS (1911), the authors pass to an examination of the alkalization hypothesis of BAKER and DODDS. From their critical survey of all this work they reach the general conclusion that tubular blockage *per se* may not be the cause of the renal symptoms, and that the blockage is itself determined by antecedent factors, of which diminished glomerular filtration due to whatever cause is an important entity since it will lead to inadequate flushing that will facilitate the deposit of material in the lumen of the tubules.

It is considered, however, that no single explanation can account for the changes in renal function and the anuria which occurs in the intravascular haemolyses, but that they are due to a series of events, starting off with the sudden haemolysis and leading to the other symptoms which are characteristic of all these conditions. The authors then proceed to consider one by one the following factors which may be involved in reducing renal function, *viz.* :—

(*a*) Effects of haemoglobin on renal metabolism.
(*b*) Haemoglobinaemia in connexion with permeability changes.
(*c*) Electrolyte-acid-base-water balances.
(*d*) Osmotic pressure in relation to filtration and reabsorption.
(*e*) Changes in glomerular filtration and tubular reabsorption.
(*f*) Urinary pigments in relation to blockage.
(*g*) Quantitative relation between tubular blockage and renal function.
(*h*) Protein catabolism in relation to azotemia.
(*i*) Favism.
(*j*) Sulphonamide haemoglobinurias.
(*k*) Crush injuries.

It is impossible in a summary of moderate length to deal adequately with this interesting and important paper. For those who are unable to consult the work in detail the following summary, given by the authors, may suffice :—

"1. The azotemia that occurs in blackwater fever, crush injuries, incompatible transfusions, favism and other intravascular haemolyses has been attributed to blockage of the renal tubules with precipitated products of haemoglobin from an acid urine with a sodium chloride content of more than 1 per cent.

"2. In the light of more recent investigation it appears that the azotemia in these conditions is of extrarenal origin, and the oliguria and anuria a result of dehydration, diminished blood volume, renal circulation and glomerular filtration. Upsets in the acid-base-electrolyte-water-balance appear to be important factors in bringing about these changes ; as a result blockage would seem to be a consequence and not a cause of the anuria ; in cases where it does occur blockage may well be an additional factor that increases the danger of renal failure. Further rising blood ureas are not necessarily an index of renal breakdown.

"3. The alkalization hypothesis is examined, and the conclusion drawn that there is insufficient evidence to warrant any statement as to its efficacy in either preventing or relieving the oliguria and anuria. It is suggested that dehydration, both actual and physiological, is a much more important factor in determining the onset of oliguria and anuria, and that more attention should be given to this aspect of the problem. It is pointed out that dangerous states of alkalaemia often result from alkalization, although the urine is still acid, and that the latter is not a sound index on which to base treatment. It is also pointed out that anuria is no commoner in "acid" than in "alkaline" patients in blackwater fever in spite of the greater haemolyses that sometimes take place in

the former. In the case of blackwater fever it should be borne in mind when assessing the value of any particular form of treatment, that 60 to 80 per cent. of the cases recover anyway, and many in the complete absence of any form of treatment.

"4. A number of recent workers have pointed out that the excretion of solids is more efficient in acid than in alkaline urine, and that the kidneys themselves retain less iron and/or pigment, which may be regarded as an index of the overloading of the tubular epithelium and of cast formation.

"5. Consistent reports show that dehydration is the most constant feature in many of the syndromes discussed above, and that tubular degeneration precedes blockage in the majority of cases.

"6. Some experimenters have concluded that blockage was the main factor in the development of the azotemia because they failed to take into account acid-base-electrolyte-water-balance disturbances, which in many cases were actually produced by the conditions of their experiments and by the administration of large doses of citrates, bicarbonates, and ammonium chlorides.

"7. The significance of hypochloraemia, and hyponatraemia is dealt with in relation to the problem of azotemia and dehydration, together with its effects on other electrolytes and the acid-base-water-balance, glomerular filtration, tubular reabsorption and urine concentration. Many workers seemed to have solved this knotty aspect of the problem to their own satisfaction by considering only one electrolyte, but the complexity of this subject becomes very evident when ionic balances are viewed as a whole, which they obviously must be.

"8. It is suggested that no single explanation can satisfactorily account for the changes that take place in renal function in the conditions described, and that they are probably due to a series of events started off by acute haemolysis.

"9. Whether haemoglobin is a toxic substance *per se* is difficult to decide in the present state of our knowledge. Many workers have reported toxic effects from injections but have failed to take into account other complicating factors. Some have stated that if the haemoglobin is stroma free no toxic effects develop; others have denied this, and by experiments have proved that neither haemoglobin nor stroma has any serious effects when injected. Others have shown that similar effects can be produced by the injection of small amounts of distilled water.

"10. In regard to incompatible transfusion there appear to be two types of reaction: (*a*) an immediate and profound reaction following the injection of very small quantities of frankly incompatible Landsteiner groups, which is generally fatal; (*b*) a less serious and somewhat delayed reaction produced by the lysis of much larger quantities of blood, producing haemoglobinaemia, methaemalbuminaemia, and haemoglobinuria, and due apparently to the presence of Rh. factors and other little known subgroups. The situation in these two conditions is compared with that in blackwater fever, and the other intravascular haemolyses. Products of antigen-antibody reaction cannot be ruled out in these conditions.

"11. It is pointed out that haemoglobin metabolism in man, dogs, cats and rabbits, etc., is not comparable, and that results of haemoglobin injection experiments into the lower animals and even into baboons, should not be lightly referred to man. Further, the interpretation of *in vitro* experiments are not always applicable *in vivo* where haemoglobin is concerned. Methaemalbumin is found in all the intravascular haemolyses of sufficient magnitude in the primates and can be produced *in vitro* by the incubation of a primate plasma-haemoglobin system provided the pH rises above 8·0. Since such a pH is never attained *in vivo* it seems that the *in vitro* and *in vivo* formations are not similar. This pigment is never found in urine, and there appears to be no quantitative relation between methaemalbumin in the plasma and methaemoglobin in the urine.

"12. There is evidence from a variety of sources to show that haemoglobin is reabsorbed by the tubular epithelium of the kidneys, and

that this in some measure accounts for the discrepancies between the amounts of haemoglobin found in the urine and that liberated by the destruction of the erythrocytes. The onset and extent of the haemoglobinuria also appears to be dependent upon the rate and capacity of the epithelial cells to take up haemoglobin from the filtrate that passes down the tubules, as well as on haemobilirubin formation.

" 13. The problem of the passage of large size molecules like haemoglobin (M.W. 17,000 × 4) through the glomerulus is discussed in the light of SVEDBERG's, MONKE and YUILE's and KEYS' work. It is suggested that several factors may be operating in this little understood phenomenon. The haemoglobin (Hb4 M.W. 68,000) molecule may dissociate into submultiples (Hb4, Hb2, Hb1) which would permit its passage through the glomerulus (SVEDBERG) in the same manner as Bence-Jones protein (M.W. 35,000) normally passes without doing injury to the glomerulus. Alternatively, the glomerulus may possess a small proportion of pores that are large enough to permit the passage of the undissociated molecule of haemoglobin ; finally, some authors suggest that changes in permeability may be a factor.

" 14. In addition to the molecular weight and radii as factors in their passage through membranes, electric charges and isoelectric points are no doubt important in controlling the passage of some molecules while retaining others. The question of permeability in general is discussed in relation to blackwater fever and the other intravascular haemolyses.

" 15. Changes in colloid osmotic equilibria of the plasma are examined in relation to glomerular filtration in blackwater fever. Insufficient data are available on this important aspect to draw any satisfactory conclusions. It has been shown that in blackwater fever the serum proteins are normal, in spite of the additional amount thrown into the plasma by the haemolysed red cells ; so that in this condition colloid osmotic changes do not appear to play a part in the onset of oliguria.

" 16. The tubular changes are examined and compared in blackwater fever, crush injuries, incompatible transfusions, post uraemic states, and after histamine and hypertonic sucrose injection, and the problem of tubular reabsorption is considered in respect of the changes that take place. Tubular changes seem to be a fairly constant accompaniment of dehydration and electrolyte-acid-base disturbances, and will have an important effect on urine formation and concentration, as well as on the back diffusion of urea. Excessive unselective reabsorption of the tubular filtrate by damaged epithelium has been suggested by some authors as a more important cause of oliguria than tubular blockage. Reduction in glomerular filtration and/or closure of glomeruli may also be a factor in tubular degeneration. H-substances, as well as the injection of histamine, have been shown to bring about tubular degeneration.

" 17. Many workers have described inclusions in the cells of the renal tubules, and recent investigators have suggested that the taking up of protein material may lead to degeneration. A further fact of importance is that in most of the conditions described there is diminished renal blood flow, due to a variety of causes, and since the oxygen consumption of the tubules is so much greater than that of the glomeruli it is likely that they would be more seriously affected by renal ischemia.

" 18. Visible glomerular changes do not appear to have been described in the conditions discussed, although more subtle changes cannot be ruled out. In the anuria due to blockage of the ureters with crystalline products of sulphonamides, glomerular changes have, however, been noted, no doubt due to back pressure as well as other factors. Some authors have described bloodless glomerular tufts in cases of incompatible transfusions and in experimental animals. It is probable that variations in renal blood flow are much more important in controlling glomerular filtration than are blood pressure changes. Variations in the number of functioning glomeruli in the mammal, although denied by some, may be a factor

in urine formation. It has been suggested that dehydration may bring this about, as it does in the frog ; here again dehydration appears to be the key to the situation.

"19. The quantitative aspects of tubular blockage are next dealt with, and the relation of this to oliguria, anuria and azotemia. Very few authors give any idea of the extent of the blockage in the cases that they examine, and confine themselves to general statements. It would appear that the extent of the blockage is, in the majority of cases, insufficient to account for the oliguria or anuria, especially when it is remembered that the kidney works with a reserve of some 80 per cent.

"20. Very little information is available concerning the relative proportions of haemoglobin and necrosed cells in the blocked tubules, nor does there appear to be much correlation between the degree of haemoglobinuria and/or blockage and anuria. In crush injuries, and incompatible Landsteiner transfusion, the amount of haemoglobin in the plasma and urine is minimal, yet oliguria, anuria and azotemia sometimes develop.

"21. The problem of urinary pigments, especially methaemoglobin, is dealt with, and the suggestion made that mere changes in pH and sodium chloride concentration are not the only factors at work in determining the amount and type of pigments present in the urine. Studies in crush injuries indicate that the pigment in the urine is met-myohaemoglobin with a molecular weight of 17,500 ; methaemoglobin has not been described in spite of the presence of oxyhaemoglobin and low pH.

"22. A brief account is given of the haemolyses that sometimes occur after sulphonamides, and in favism, and the suggestion is made that these probably fall into the same category as the other intravascular haemolyses."

W. Yorke.

TRYPANOSOMIASIS.

VAN HOOF (L.), HENRARD (C.) & PEEL (E.). Recherches sur le comportement du *Trypanosoma gambiense* chez le porc. [**The Behaviour of** *T. gambiense* **in the Pig.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 53–68.

Certain observations made at the Léopoldville laboratory have led to the conclusion that the indigenous pig may be an ideal reservoir of the trypanosomes pathogenic for man [this *Bulletin*, 1938, Vol. 35, p. 330]. Although they are very rare in the blood, trypanosomes readily infect Glossina. The infected pig remains asymptomatic for prolonged periods. After three cyclical passages through the pig, *T. gambiense* preserves its pathogenicity for man.

Full details of this work, which has been going on for more than two years, are given in the present paper. The following is the summary :—

1. A strain of *T. gambiense* remains pathogenic for man after 3 and after 10 cyclical passages in pigs.

2. The index of transmissibility of this trypanosome was at first exalted during its initial cyclical passages through the pig, but later gradually decreased. The introduction of another vertebrate host exalted it. The attenuation is attributed to the persistence of the trypanosome in a single species of animal and to the benign character of the affection produced.

3. During the evolution of the infection in the pig, the cyclical transmissibility of the trypanosome gradually became attenuated.

4. *T. gambiense* produces an asymptomatic affection in the pig, which evolves towards spontaneous cure. Reinfection is possible, even with the same strain. In the course of reinfection the transmissibility is conserved in certain cases, but on the whole it is diminished and sometimes it is lost. Reinfection produces an infection which is shorter and more discrete. It may even be impossible owing to the immunization of the animal. There is no immunity against heterologous strains such as *T. brucei.*

The first infection manifests itself most frequently by the appearance of trypanosomes in the blood during a variable period, but this period may be entirely absent, and in such cases the presence of the parasite can only be discovered by haemoculture or by xenodiagnosis. The animal is nevertheless infectious. During the second period the parasites are no longer discoverable by direct observation, but the animal remains infectious for a period, which may be at least a year.

5. In the course of successful cyclical passages through 10 pigs, one strain of *T. gambiense* has not shown any notable change in respect of morphology or of chemo-resistance. *W. Yorke.*

VAN HOOF (L.), HENRARD (C.) & PEEL (E.). Irrégularités de la transmission du *Trypanosoma gambiense* par *G. palpalis.* [**Irregularities in the Transmission of** *T. gambiense* **by** *G. palpalis.*]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 69–80. [16 refs.]

Previous work by these authors has shown that although a single bite from an infective Glossina usually infects the guineapig, it fails to do so in about 7·7 per cent. of cases [this *Bulletin,* 1938, Vol. 35, p. 335]. Various hypotheses have been advanced to explain this phenomenon, *viz.,* (1) a transient refractory state on the part of the guineapig ; (2) a loss of virulence of the trypanosome for the vertebrate ; and (3) a diminution in the infective power of Glossina, possibly because the salivary glands have been freed from parasites, possibly because the salivary trypanosomes have been affected by feeding on animals which have received drugs, possibly because of some anatomical imperfection in the biting apparatus and salivary tract, and possibly because the salivary trypanosomes in the course of their development pass through phases in which they cease to be pathogenic.

In the present paper the authors have examined the problem in considerable detail, and as the result of their investigations with isolated infected Glossina they have reached the following conclusions :—

In a strain of *T. gambiense* taking well on the guineapig, each bite causes infection.

In another strain less well adapted, there are failures. These failures increase when the Glossina are fed on animals which have been treated by Germanin, even when the interval between the administration of the drug and the infecting meal is very long, surpassing the average duration of the protection conferred by the drug.

Evidence of an enfeebled capacity of trypanosomes to infect Glossina is seen in the prolongation of the incubation period. This was extended to 86 days for the last bite of an isolated fly on the 103rd day of the life of this fly.

A record is given of the history of a Glossina which, after having infected an animal, was completely cleared of all flagellates.

The influence of feeding infective flies on fowls appeared to be very doubtful.

Anatomical malformations of the salivary or biting apparatus of Glossina were not observed by the authors.

Observation of guineapigs subjected to the bites of isolated infective Glossina indicates without doubt a transient refractory state in certain of the vertebrate receptors. But it is possible to find other explanations, of which an important one is a delay in the completion of the cycle of the parasite in the fly. This very plausible hypothesis, however, cannot explain all the failures.

Finally, the capacity of the trypanosomes to infect the guineapig can be altered or even suppressed. It was totally suppressed in a strain of *T. gambiense* which had sojourned for almost 10 years in the same patient. This prolonged sojourn, or possibly the various treatments which the patient received, must have produced this modification. In other strains of *gambiense* coming from a patient infected for a long time or from one in whom the disease developed very slowly, the same change, although in a less degree, was observed and could not be explained as the result of drug-treatment. The loss of virulence for the guineapig of the salivary trypanosomes in flies infected from the pig, which shows few signs of disease, is very marked.

W. Yorke.

BURTT (E.). **Observations on the High Proportion of Polymorphic Trypanosome Infections found in the Salivary Glands of** *Glossina brevipalpis* **near Amani, Tanganyika Territory, with a Note on the Appearance of the Infected Glands.**—*Ann. Trop. Med. & Parasit.* 1942. Dec. 31. Vol. 36. No. 4. pp. 170–176. [13 refs.]

From April to December 1937, Burtt was engaged in investigating the ability of *G. brevipalpis* to transmit *T. rhodesiense*. Concurrently with these transmission experiments, numbers of *G. brevipalpis* were dissected and their salivary glands examined. The preliminary dissections were found to yield such an unusually high proportion of positive results that this aspect of the matter was further investigated. The results are recorded in the present paper. In all, 12,550 male *G. brevipalpis* were dissected and 105 (0·84 per cent.) were found to have salivary gland infections. Details are given of the localities studied in the present investigation and the results are recorded in tables.

The following is the summary :—

"1. A total of 12,550 *Glossina brevipalpis* were dissected from three localities near Amani, Tanganyika Territory, and 105 flies were found with salivary gland infections. The results from the three localities were as follows : (*a*) at Sigi 2,217 flies were dissected, of which 0·32 per cent. were infected ; (*b*) at Old Road 3,008 flies were dissected, of which 0·73 per cent. were infected ; (*c*) at Masherwa 7,325 flies were dissected, of which 1·04 per cent. were infected.

"2. The infected salivary glands in *G. brevipalpis* appeared chalky-white by reflected light and could be recognized with the naked eye.

"3. A large proportion of the infected salivary glands in *G. brevipalpis* appeared Vandyke brown or black when viewed under the lower power of the microscope. These seemed to be old infections. Others lacked this dark appearance and were probably young stages of the infection in the gland.

"4. Most of the salivary gland infections in *G. brevipalpis* were extraordinarily heavy. This conforms with the findings of Bruce *et al.* in Nyasaland. Only three light infections were observed.

"5. Of the 105 flies with infected salivary glands, 43 also had trypanosome colonies in the labrum.

"6. Marked fluctuation in the proportion of flies with infected salivary glands occurred over short periods ranging from 1 to 18 days. The percentage of infected flies varied from 0 in 582 consecutive flies examined to 4·94 in a batch of 81 flies. Very large samples, therefore, need to be examined before a representative picture is obtained for any locality.

"7. No relationship was noted between the mean monthly maximum temperature recorded at Sigi and the proportion of flies with infected salivary glands which occurred there, although the greatest proportion was observed in the locality with the lowest altitude and therefore with the warmest general climate."

W. Yorke.

LOURIE (E. M.). **Treatment of Sleeping Sickness in Sierra Leone.**—*Ann. Trop. Med. & Parasit.* 1942. Sept. 30. Vol. 36. No. 3. pp. 113–131. [20 refs.]

In this paper the author records the results obtained by him in the treatment of *gambiense* sleeping sickness by the aromatic diamidines. The work was carried out in the Kailahun district of Sierra Leone from September 1939, to July 1941. The outbreak was apparently of four to five years' duration and in parts of the area the infection rate was as high as 20 to 30 per cent. The patients were treated in the course of control of the outbreak by mass-diagnosis and mass-treatment by mobile teams in the field. The great majority of the patients were treated by the well-established remedies antrypol and tryparsamide, but opportunity was also taken to test certain of the aromatic diamidines. Among the 3,197 patients dealt with, 95 per cent. were in fair condition, but the remainder showed evidence of serious affection, *i.e.* gross somnolence, dementia, severe pituitary-thyroid derangement, inability to walk without support, etc. The mortality among untreated cases was estimated to be as high as 300 to 350 per 1,000 per annum. The patients belonged mainly to the Kissi tribe and were very poor and undernourished. Their diet consisted of little else than rice and they were regularly subject to a severe "hungry season" during the months preceding the annual rice harvest. The hungry season of 1940 was particularly serious, amounting practically to a period of true famine. Lourie states that these factors probably predisposed towards the severe toxic effects of treatment by antrypol and tryparsamide—toxic effects which were more severe than those reported elsewhere.

Twelve different treatment courses were employed. The drugs were usually given intravenously but occasionally intramuscularly. They were dissolved in freshly distilled water. The average weight of adult patients was about 118 lb. for males and 105 lb. for females; children were given fractional doses on a basis of full adult doses per 100 lb. of body-weight. The treatment courses were as follows:—

"*Antrypol or tryparsamide alone*

(i) Antrypol, 5 doses of 1 gm.; at five-day intervals.
(ii) Tryparsamide, 10 doses of 2 gm.; at five-day intervals.

"*Combined courses of antrypol and tryparsamide*

(iii) Antrypol, 3 doses of 1 gm., followed by tryparsamide, 5 doses of 2 gm.; at five-day intervals.
(iv) Antrypol, 3 doses of 1 gm., followed by tryparsamide, 7 doses of 2 gm.; *five- or seven-week interval between the first two doses*, then five-day intervals.

(v) Antrypol, 2 doses of 1 gm., followed by tryparsamide, 6 doses of 2 gm.; at five-day intervals.
(vi) Antrypol, 1 dose of 1 gm., followed by tryparsamide, 9 doses of 2 gm.; at five-day intervals.

" *Aromatic diamidines*

(vii) Stilbamidine,* 8 doses of 50 or 75 mgm.; usually daily, but sometimes at five-day intervals.
(viii) Pentamidine,* 8 doses of 50 or 75 mgm.; usually daily, but sometimes at five-day intervals.
(ix) Pentamidine, 10 doses of 100 mgm.; at five-day intervals.
(x) Pentamidine, 12 doses of 100 mgm.; daily.
(xi) Pentamidine, 3 doses of 50 mgm., followed by tryparsamide, 5 doses of 2 gm.; at five-day intervals.
(xii) Propamidine,* 8 doses of 50 or 75 mgm.; usually daily, but sometimes at five-day intervals."

Lourie deals in some detail with the toxic effects of treatment. Immediate reactions to antrypol and tryparsamide were usually quite inconspicuous, but a number of complaints were very apt to arise a few days after injection. These were, more or less in order of frequency :—

" *After antrypol* : headache and generalized body-pains; fever; cough or bronchitis; diarrhoea; stomatitis, gingivitis or sore throat; papular rashes; localized oedema, generally of legs or face but sometimes in other sites, such as arms or scrotum; peeling of skin, generalized or especially around the mouth; blepharitis or conjunctivitis; jaundice; itching of skin.

" *After tryparsamide* : visual disturbances, such as dimness or blurring of vision; headache and body-pains; cough; diarrhoea; fever; peeling of skin; papular or maculo-papular rashes; itching; sore throat; lachrymation; oedemas.

" *After three doses of antrypol followed by tryparsamide* : severe body-pains and headache; fever; diarrhoea; stomatitis or gingivitis, and occasionally herpes; peeling of skin, usually branny but often exfoliative; oedemas; cough; visual disturbances; papular or maculo-papular rashes; blepharitis or conjunctivitis, sometimes suppurative; vomiting; itching; jaundice."

The general similarity of these symptoms suggests that they are for the most part not referable to any essential toxicity of either drug in the absence of some common underlying unfavourable factors such as those mentioned above, but it is noteworthy that they did not arise among patients treated by the diamidines. The toxic effects occurred in about 20 per cent. of 148 cases treated by five antrypol doses with no tryparsamide, and in about 10 per cent. of 485 cases treated by 10 tryparsamide doses with no antrypol. They were usually mild, but were sufficiently serious to require treatment to be interrupted in each group in about 3 to 5 per cent. of cases, with less than 1 per cent. of deaths during treatment or within a month of its termination. In the combined treatment of course iii (three injections of antrypol followed by five of tryparsamide, with five-day intervals between all doses) the incidence of toxic complications among the 1,466 patients was considerably higher, *i.e.* 35 per cent., including 15 per cent. serious, with a mortality of as much as about 5 per cent. during treatment or within a month of its termination.

* The names stilbamidine, pentamidine and propamidine have been given recently to 4 : 4′-diamidino stilbene, 4 : 4′-diamidino diphenoxy pentane and 4 : 4′-diamidino diphenoxy propane respectively.

In course v, (two doses of antrypol followed by six of tryparsamide, with five-day intervals between all doses) the incidence and severity of toxic effects seemed to be only slightly less. Considerably fewer and milder toxic reactions were, however, encountered in course iv, consisting of three doses of antrypol followed by seven of tryparsamide with five or seven weeks between the first two doses and then five-day intervals, and in course vi, consisting of one dose of antrypol followed by nine of tryparsamide with five days between all doses. The fact that course vi should have been so much less toxic than course iii is particularly striking in view of the fact that it involved the injection of nearly twice as much tryparsamide. After considering his observations on this matter, Lourie reaches the conclusion that where there was an interval of five days between all injections, a course of three antrypol followed by tryparsamide was associated with very severe toxicity; he believes that a preliminary dose of antrypol five to seven weeks previously is able, whether by improving the condition of the patient or in some other way, to mitigate the toxic effects of later courses of antrypol followed by tryparsamide at five-day intervals.

A table shows the relationship of cerebrospinal fluid cell count at the start of treatment to incidence of serious visual disturbance after treatment. The incidence of serious visual complications after tryparsamide varies from less than 0·5 per cent. to nearly 6 per cent. according to the initial cell count.

Turning to the diamidines, Lourie found that the outstanding feature of the immediate reaction is the sudden and usually severe but transient fall in blood-pressure. Associated with this there may be a number of subjective and objective disturbances. With the sudden drop of blood-pressure there was a rapid, thin or imperceptible pulse, sweating, dizziness, faintness or loss of consciousness, sometimes with epileptiform twitchings and, on rare occasions, incontinence of faeces and urine. Salivation with nausea was common, and sometimes vomiting. There was also often a curious puffy suffusion of the face and eyelids. Within 10 minutes to half an hour the patients recovered from these disturbances, apparently completely, in all cases. No late toxic effects visual or other, were observed after the administration of the diamidines.

The next portion of the report deals with the effects of treatment. These are summarized in a series of tables. The following are the conclusions :—

" 1. Conclusions are drawn upon the effects of the treatment of *T. gambiense* sleeping sickness, among people of a particularly poor and undernourished type, in Sierra Leone from September, 1939, to July, 1941. Treatment was mainly by antrypol and tryparsamide, but the opportunity was also taken to make a trial of three aromatic diamidines—pentamidine, propamidine and stilbamidine.

" *Toxicity*

" 2. Treatment by antrypol (1-gm. doses) and tryparsamide (2-gm. doses) was frequently followed by severe toxic effects. These arose in cases treated by either drug alone, but were of particularly high incidence and severity in a combined course of 3 antrypol doses followed by 5 tryparsamide, all injections being at five-day intervals. Such a combined course was more severely toxic than a regimen of only 1 antrypol followed by 9 tryparsamide doses, at five-day intervals, in spite of the fact that the latter course involved the injection of nearly twice as much tryparsamide. There is some evidence to suggest that the toxic effects of a combined

course of several antrypol followed by tryparsamide injections, at five-day intervals, may to some extent be mitigated by the preliminary injection of a dose of antrypol 5–7 weeks before the beginning of the course.

"3. After treatment by tryparsamide, or by antrypol followed by tryparsamide, the incidence of serious visual disturbances varied from less than 0·5 per cent. of 318 cases in whom there had been 0–4 cells per c.mm. in the cerebrospinal fluid at the start of treatment to nearly 6 per cent. of 102 cases in whom the initial count had been over 100 per c.mm.

"4. Injections of the aromatic diamidines usually produced severe and often alarming immediate reactions, associated with a pronounced fall in blood-pressure but passing within half an hour. There were no later toxic effects comparable with those encountered after antrypol and tryparsamide, and in fact no late toxic result of any nature, visual or other. It is a distinct advantage of these compounds over antrypol and tryparsamide that they may be given in daily injections—the most intensive course employed was of 100 mgm. pentamidine daily for 12 days, and this was given to 80 cases. However, reference is made to the reports of other workers which indicate that, in heavier dosages than were practicable for the Sierra Leone cases, the aromatic diamidines are not without potentiality of producing late toxic disturbances of a serious nature.

"*Therapeutic Value*

"5. Figures are given showing the proportion of cases in which, 5–6½ weeks and 4–5 months respectively after the start of treatment by different types of course, there was a change in the cerebrospinal fluid cell count of the following order:

(*a*) An increase to more than 10, where the count at the start of treatment had been 0–4 per c. mm., or to more than double the initial count where this had been above 4 per c. mm.

(*b*) A decrease to less than the square root of the count at the start of treatment where this had been above 20 per c.mm.

"It is, of course, not suggested that such an increase or decrease in the cell count after treatment is *in any individual case* necessarily of great prognostic significance, but in sufficiently large groups treated by different means valuable inferences are to be obtained by comparing the relative numbers of cases in which these changes have occurred.

"6. The changes in cerebrospinal fluid cell counts, together with the results of a clinical follow-up investigation 12–20 months after treatment, warrant the conclusions that:

(*a*) In early cases the curative properties of pentamidine and of propamidine are no less than those of tryparsamide (the latter drug given either alone or preceded by injections of antrypol). Stilbamidine is of considerably less value.

(*b*) In late cases tryparsamide is much more effective than the three diamidines named."

W. Yorke.

FAIN (Alexandre). Accidents toxiques et résultats après une seule injection de Bayer 205 administrée préventivement dans un ancien foyer de trypanosomiase. [**The Toxic Effects and the Results of a Single Injection of Bayer 205 Administered as a Preventative in an Old Focus of Trypanosomiasis.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 137–144.

The observations described in this paper were made among the population living on the Congo between the Kasai river and Stanley Pool. The population numbered about 4,500 individuals, almost all of whom received an injection. The focus of sleeping sickness was very old but still active; during 1939, 162 new cases (3·69 per cent. of the total population) were discovered.

The drug employed was Belganyl Meurice. It was given in a dose of 0·025 gm. per kilo., dissolved in six times its weight of distilled water. The German preparation Bayer 205 was administered to 20 patients, with the object of comparing its toxic effect with that of Belganyl; no difference was discovered. The toxic effects were noted and have been grouped as follows :—

Toxic effects occurring immediately or very early. In many patients a condition of presyncopal nausea was noted within a few minutes of the injection; it was very transient. In about a dozen cases this was accompanied by marked shock and vomiting. At the beginning of the crisis there was often transient congestion of the face and sometimes of the whole body. A fatal issue was observed in a woman of 45 years who received only 1 gm. of Belganyl. She exhibited in a marked degree the symptoms described, and some moments before death the sphincters were relaxed, with the passage of urine and faeces. It is interesting to note that all subjects, except one, in whom the circulatory shock was intense, were adult women. Another sign observed immediately after injection was a cutaneous eruption. Often within an hour there appeared large or small papules; sometimes there was itching of the skin and there was usually a rise of temperature.

Toxic effects appearing some hours after the injection or on the following day. These were :—

(1) Papular eruptions, which might or might not itch.

(2) Two to three hours after the injection a large number of patients had a febrile disturbance, usually short but often serious; in many cases the temperature was over 40°C.

(3) Intense photophobia with lachrymation was observed the day after the injection.

(4) Palpebral oedema was seen in one patient the day following the injection.

(5) Intense abdominal distension accompanied by constipation was seen in a baby of five months.

(6) The majority of the individuals injected exhibited a cutaneous hyperaesthesia which was very marked and localized in the extremities of the limbs. This phenomenon appeared the day after, or the day but one after, the injection, causing difficulty in walking and preventing manual work. This was due to localized hyperaesthesia of the soles of the feet and palms of the hands.

Toxic effects appearing some days after the injection. The chief of these was albuminuria. Examination of the urine of 46 patients who had received 1·5 gm. of the drug showed that the toxic action of Belganyl and of Bayer 205 is far from negligible. In several patients the albuminuria reached 2 gm., and microscopic examination of the urine revealed casts and red cells.

Toxic effects about a week after injection. Towards the end of the first week a number of patients showed a cutaneous desquamation localized in the extremities of the limbs.

The author made some observations on the results of prophylactic administration of Belganyl after a nine months' interval. It was intended to give four injections at three-monthly intervals during the year 1940, but for various reasons the May and August injections were not given. There was thus a period of nine months between the first injection given in February and the second at the end of November. After the injection in February 1940, the population was visited three times, *viz.*, in May, August and November. On each occasion every

individual was carefully examined from the point of view of trypanosomiasis. Details are given of twelve new cases discovered in the course of these three visits. All these patients had received the preventive injection of Belganyl in February 1940. It is interesting to note that only three of these 12 patients had trypanosomes in the blood or glands, and also that a large proportion of them were in an advanced stage with grave clinical symptoms and a profoundly changed cerebrospinal fluid. The general conclusion drawn from this work is that the wholesale administration of Belganyl is not without dangers. The toxic effects are not negligible, but the real advantages resulting from the procedure in a heavily infected district largely compensate for its defects. *W. Yorke.*

IRIARTE (David R.). Xenodiagnóstico y reacción de Machado Guerreiro en la enfermedad de Chagas. [**Xenodiagnosis and the Machado-Guerreiro Reaction in Chagas's Disease.**]—*Bol. Laboratorio Clinica "Luis Razetti."* Caracas. 1941. Aug. Vol. 2. No. 5. pp. 102–107.

This is a very iconoclastic paper. The author dilates upon the difficulties of carrying out the xenodiagnostic test unless all laboratory facilities and a good insectarium are available. In hospital and general survey work the difficulties are almost insuperable and, judging from his personal experience, he has not been very successful. He has carried out the test on 35 patients, using larvae and nymphs of *Rhodnius prolixus* and *Eutriatoma maculata*, the former for 24 and the latter for 11. Of the patients 27 were males, 8 females; twelve were under 20 years of age, thirteen between 20 and 30, seven between 30 and 40, and three between 40 and 50. They came from thirteen States; 4 were whites, 5 natives, and 26 were half-castes. They presented one or more symptoms of Chagas's disease—fever, splenomegaly, hepatomegaly, cardiac lesions or irregularities, adenopathy, nervous disturbances, anaemia, etc. All were negative to the xenodiagnostic test.

Twenty-eight were subjected to the Machado-Guerreiro reaction. Two were positive, one strongly, one weakly, and a third was doubtful. The author concludes: "The Machado-Guerreiro reaction is losing ground. It is not a specific reaction but a group one and is given also by leishmanial conditions, which are common in this country."

H. Harold Scott.

LEISHMANIASIS

PELÁEZ REDONDO (Julio). Die Hämatologie der Kala-Azar der Erwachsenen. Diagnostische Bedeutung der Sternalpunktion. [**Haematology of Adult Kala Azar. Diagnostic Value of Sternal Puncture.**]—*Wien. Klin. Woch.* 1942. July 24. Vol. 55. No. 30. pp. 585–588. With 1 fig. [32 refs.]

The author, who has been studying kala azar in Spain, calls attention to the fact that since the civil war cases have become increasingly common in adults. There does not seem to be any satisfactory explanation of this increase in the adult incidence, but it must in some way be connected with the breakdown in the sanitary system as a

result of the war. A similar increase in adult cases has been reported in recent years from other Mediterranean countries. A number of such cases were studied by the author in Salamanca. He has found that spleen puncture is the surest method of discovering leishmania. Sternal puncture is free from risk but is less likely to reveal the parasites, while in no case has he been able to demonstrate leishmania in the blood. In 16 of a series of 17 cases there was a marked leucopenia. The one exception was in a case of only a week's duration. The leucopenia is due to a decrease in the granulocytes, which causes a relative lymphocytosis, though there was no change in the absolute number of lymphocytes. The granulocytes present in the blood are largely immature forms with 4 per cent. myelocytes and 8 per cent. unsegmented forms. In many cases the eosinophiles are diminished. There is an increase in the monocytes and plasma cells. In all cases a marked thrombocytopenia existed. The bone marrow showed changes corresponding with the altered blood picture, as shown in the myelograms from four of the cases, which are reproduced in the paper. The author concludes that the cases studied indicate that the bone marrow has been influenced by the changes occurring in the spleen as well as by the toxic action of the parasites leading to an increased passage of cells into the peripheral blood. *C. M. Wenyon.*

BARBER (H. J.), SLACK (R.) & WIEN (R.). **Increase in Toxicity of Stilbamidine Solution on Exposure to Light.** [Correspondence.]—*Nature.* 1943. Jan. 23. Vol. 151. No. 3821. pp. 107–108.

KIRK in a private communication to the reviewer suggested that solutions of stilbamidine which had been kept for some time increased in toxicity and that this fact explained a number of deaths which had occurred after the use of this drug in the treatment of leishmaniasis in the Sudan. FULTON and YORKE [this *Bulletin*, 1943, Vol. 40, p. 23] investigated the point, and found that solutions of stilbamidine which had been exposed to light increased considerably in toxicity for mice, whereas solutions which had been kept in the dark remained unchanged. The present work has confirmed and extended these observations.

It was found that dilute solutions of stilbamidine (0·5 per cent.) exposed to sunlight increased in toxicity four- to five-fold in about four days, after which there is no appreciable further increase. Weak solutions changed much more rapidly than did stronger solutions, but by subjecting 10 per cent. solutions to the light from a mercury arc lamp for several hours the authors have been able to prepare sufficient quantities of toxic solution for isolation of the material responsible for this toxicity. It is believed that the toxic product is almost certainly 4 : 4′-diamidino phenyl benzyl carbinol, but rigorous proof is difficult. It is probable that the reaction occurring in aqueous solution is an addition of the elements of water to the double bond of the stilbene linkage. It follows from this and from the fact that other therapeutic diamidines have shown no such alteration in biological or chemical properties, that the change is associated solely with the unsaturated stilbene linkage and that the amidine groups are not affected.

The symptoms produced in mice by the toxic substance were more stimulant in character than those caused by freshly prepared solutions of stilbamidine, which were mainly depressant. In general, the pharmacological effects shown by the toxic product differed quantitatively rather than qualitatively from those of the original substance. The

depressor action in the anaesthetized cat was increased about five times, and recovery was delayed. Atropine only partially antagonized this effect, while the spleen was actively contracted. Smooth muscle of the rabbit intestine was sometimes contracted in concentrations of about 1 in 50,000, but after atropine, inhibition and relaxation were always produced; this differed from the effect of stilbamidine, which caused contractions which were only slightly reduced after atropine. The fall of pressure was probably mainly due to vasodilatation since there was no depressant action on the isolated rabbit's heart. The isolated product had a toxicity in mice which was five times greater on intravenous injection and 10 times greater on subcutaneous injection than that of stilbamidine. It is important to note that the toxic product was almost inactive therapeutically against *T. equiperdum*.

W. Yorke.

KIRK (R.). **Some New British Synthetic Drugs in the Chemotherapy of Protozoal Infections.**—*East African Med. Jl.* 1942. Oct. Vol. 19. No. 7. pp. 219–223. [24 refs.]

In this note, Kirk briefly summarizes results obtained in the clinical trial of the aromatic diamidines in trypanosomiasis, leishmaniasis and babesiasis. All this work has already been summarized in this *Bulletin*. *W. Yorke.*

SILVERBERG (Mabel G.) & HENSCHEL (Egbert J.). **Oriental Sore in the United States. Report of a Case.**—*Arch. Dermat. & Syph.* 1942. Nov. Vol. 46. No. 5. pp. 705–710. With 3 figs.

The case reported is that of a man 48 years of age who developed oriental sore in the form of lesions on the forehead, ear and wrist a few months after returning to the U.S.A. from a visit to Greece. Leishmania were demonstrated in the lesions, which disappeared after 41 intravenous injections of a 1 per cent. solution of tartar emetic.

C. M. Wenyon.

GELBER (A.). **Oriental Sore Possibly Contracted in the United States. Report of a Case.**—*Arch. Dermat. & Syph.* 1942. Nov. Vol. 46. No. 5. pp. 739–740.

A woman, 53 years of age, a native of California, noticed a small red papule on the middle of the left check 12 years after a visit to Italy. The lesion increased in size and was finally removed by surgical diathermy. It is stated that "examination of the infiltration with the Gram stain shows the presence of leishmania bodies (*Leishmania tropica*)". It is concluded that if the patient became infected during the European tour an incubation period of 13 years must be admitted. On the other hand, if infection did not then take place it must have occurred in the U.S.A., probably from contact with natives from the Near East. [The evidence that the parasite was actually *Leishmania tropica* seems inconclusive as Gram staining is not the usual method for demonstrating this organism.] *C. M. Wenyon.*

ROW (R.) & KULKARNI (S. S.). **The Rôle of Methaemoglobin on the Leptomonad Phase of *Leishmania tropica*, with Special Reference to its Reversion into Leishmania Forms in Culture.**—*Indian Med. Gaz.* 1942. Sept. Vol. 77. No. 9. pp. 536–537. With 6 figs. on 1 plate.

In a former publication [this *Bulletin*, 1923, Vol. 20, p. 103] Row showed that in old cultures of *Leishmania tropica* there appeared rounded leishmania forms of the parasite which he styled O-bodies. To the presence of these forms he attributed the infectivity to mice of old cultures even to the extent of producing generalized infections as in kala azar. Studying the production of the leishmania forms in old cultures, the authors have found that their appearance coincides with the transformation of the oxyhaemoglobin of the medium into methaemoglobin. To test the influence of methaemoglobin on the flagellate forms the following procedure was adopted: The liquid of an old culture in which the change had occurred was centrifuged and the brown supernatant fluid separated. Into this fluid, containing methaemoglobin, actively multiplying flagellates from a young culture were inoculated. Active multiplication with rosette formation continued, but after about a week's growth increasing numbers of leishmania forms began to appear. A study of smears shows that the leishmania forms are the result of a shortening of the flagellate forms in the rosettes with, finally, a retraction of the flagella. *C. M. Wenyon.*

AVERY (Harold). **Treatment of Oriental Sore: a Review of Recent Literature.**—*Jl. Trop. Med. & Hyg.* 1942. Aug. 15. Vol. 45. No. 16. pp. 121–124. [39 refs.]

FEVERS OF THE TYPHUS GROUP.

BIRAUD (Yves). La menace actuelle du typhus exanthématique en Europe et les possibilités d'y parer.—Reprinted from *Bull. de l'Organisation d'Hygiène de la Société des Nations.* 1942. Vol. 10. Extrait No. 1. 85 pp. With 1 chart & 1 map. [Bibliography.]

——. **The Present Menace of Typhus Fever in Europe and the Means of combating it.**—*Bull. Health Organisation.* (League of Nations.) 1943. Vol. 10. No. 1. pp. 1–64. With 1 chart & 1 map. [Bibliography.]

This valuable Bulletin on louse-borne typhus in Europe deals with the existing epidemiological conditions, the possibility of an extension of the disease, and the steps that can be taken for its control by disinfestation and the use of vaccines.

The devastation that can be caused by typhus is shown by the experience of Eastern and South-Eastern Europe during and after the war of 1914–18.

TARASSEVITCH estimated that 25 million cases occurred in Russia in the years 1917 to 1921, not including the millions of "inapparent" attacks in children and partly-immune adults. The remarkable freedom of the Western Front in 1914–18 is attributed to absence of the virus from the civil population.

In the discussion of recent events the author holds that the reason why the campaign in Poland was not immediately followed by an epidemic was that it occurred in September, the month in which infection is at its lowest ebb. In the six months ending June 1940, however, there were nearly 4,000 cases in the Warsaw district against only 33 in the corresponding period of the previous year. The disease has been increasing in the same way all over Poland and in the Balkan countries. Even more ominous is the experience in Germany, where there were no cases in the civil population in 1939 ; 6 in 1940 ; 395 in 1941 ; and 1,732 in the first half of 1942. No further figures are being published in Germany and there is no information about the incidence of the disease among troops or prisoners of war in the Reich or occupied countries. Infection has been widespread in Germany ; it has presumably been introduced by prisoners and by soldiers returning from the eastern front. No official information is available from Soviet Russia, but although conditions in Russia are specially suitable for the occurrence of outbreaks the Russian troops have a great advantage over the German in being partly immunized by previous attacks.

Spain was surprisingly free from typhus during the civil war but there have been many post-war epidemics in various parts of the country. In the first three months of 1942 there were 3,604 cases, nearly half of them in Madrid and Barcelona.

Typhus is endemic in all the countries of North Africa : epidemics are closely associated with periods of economic distress. In Morocco Blanc's vaccine is said to have controlled the disease, but in Algeria and Tunisia the cases in 1941 were more than double those recorded in any of the previous twenty years, and in 1942 were even more numerous.

[In *Public Health Reports*, Washington, the cases from January to September 1942 are shown as follows : Morocco, 25,666 ; Algeria, 34,913 ; Tunisia, 16,152 ; and Egypt, 22,653. These figures do not bear out the statement that the disease has been brought under control by vaccines in Morocco.] French observers hold that many of the cases are old infections which have remained dormant and have been lighted up by malnutrition.

Isolated cases have been occurring in France among new arrivals from North Africa and also in domiciled labourers originally from the same region. The disease has spread only in the prisons of Marseilles, in which more than 100 cases have occurred.

If the war is prolonged so as to cause widespread economic distress a great epidemic can only be prevented by the strict control of louse infestation in the civil and military population. Among the precautionary measures are ; the education of medical personnel, especially in early diagnosis ; the isolation of patients ; the provision of stocks of vaccine and of an organization for collecting convalescent serum or for preparing hyperimmune animal serum.

The section on vaccines is of special interest ; about two-thirds of the text is devoted to the subject. A clear and succinct account is given of every important type of vaccine, and information is given about some recent developments which have not yet been published.

The great advantage of killed vaccines is their complete safety, but the maximum degree of immunity takes three weeks to a month to develop ; three injections are needed ; protection lasts only for about one year and is to some degree specific for the strain of Rickettsia from

which the vaccine is prepared. Living vaccines are all prepared from murine strains of Rickettsiae but they give an earlier and higher degree of protection, and that with a single injection. On the other hand many workers fear that the introduction of a living virus may give rise to an infection which is capable of being transmitted by lice, and a certain number of accidents, some of them fatal, have followed their use. Recently efforts have been made to titrate their virulence so as to avoid the use, on the one hand of ineffective, and on the other of dangerous strains.

Of the killed vaccines, Weigl's has largely fallen into disuse: in Weigl's laboratory each dose costs about three Swiss francs.

Cox's vaccine, made from *R. prowazeki* cultivated in the yolk sacs of chick embryos, is being made in large quantities in the U.S.A. and used for the protection of American troops as well as for export to England and other countries. It has also been adopted by the German army, and is being made in China and South Africa. Three doses are given at intervals of seven to ten days, followed by single doses every four to six months. Conclusive evidence of its efficacy in field conditions is not yet available.

Killed vaccines made from the lungs of mice and other rodents inoculated by the nasal route are being prepared in Paris, Algeria, Zurich, Tunis, Bucharest and Germany. CIUCA has just reported good results in Rumania. Most of the laboratory workers engaged in its preparation get attacks of the disease. In Zurich MOOSER uses the murine strain of Rickettsiae, elsewhere the classical strain is used.

The egg-yolk and rodent-lung vaccines give equal protection to animals, but their comparative efficacy in the field is not yet known.

Living vaccines are always made from the murine strain of the virus. Both of the original methods of preparation, by BLANC and LAIGRET, have been superseded because of "incidents" that arose during their large-scale application in North Africa.

Blanc now uses a vaccine made from the bile-treated faeces of fleas infected by feeding on white rats inoculated with the virus. The vaccine is supplied in the dry condition; it keeps well and can be used by any physician.

LAIGRET and DURAND now make a living vaccine from the brains of mice inoculated by the intraperitoneal route. The dose is titrated by finding the amount needed to cause paralysis in mice. From one mouse's brain a thousand doses can be prepared. Claims are made by their authors that these new living vaccines are quite safe, but there has been a general reluctance on the part of other workers to use a living virus whose later behaviour in the human body cannot be predicted.

The preventive measures against typhus can be summed up as: disinfestation, which if properly carried out, gives complete protection to any community, and vaccination by one or other method according to circumstances. In limited outbreaks in a stable and non-infested population, killed vaccines are recommended: in widespread epidemics living vaccines must be used because they alone can give prompt protection and the risks involved are far less than those of the disease.

[This Bulletin is invaluable to all those who are interested in the prevention of louse-borne typhus. The author has discussed, frankly and fully, the limitations of prevention by vaccines, but it may be well to warn the uninitiated that disinfestation is the only method that has been proved to be completely effective. The personnel engaged in

prevention must be inoculated and, even more important, must be youthful; troops going to infected places must also be inoculated, but disinfestation, whenever practicable, is just as essential as ever. Vaccination should be regarded as a subsidiary method of control, though in exceptional circumstances it may be the only practicable measure. Cox's is the only vaccine likely to be available.]

John W. D. Megaw.

CIUCA *et al.* **Contributions to the Study of the Virulence of** *Rickettsia prowazeki.*—*Bul. d. l. Sect. Scient. d. l'Acad. Roumaine.* 1941. Vol. 24. No. 3.

The following is a translation of a German abstract of the paper dealt with:—

A Rickettsia strain was obtained from inoculation of guineapigs with blood of typhus patients and then enriched by intra-anal instillation of brain emulsion from the guineapig into the louse gut. This strain showed an exceptional virulence for human beings, which was retained even after 24 passages. The risk of infection in the laboratory for persons handling it was 100 per cent. The disease attacked the body by way of the mucous membrane or quite insignificant skin lesions. Persons who had not previously been inoculated against it suffered the severest attacks of the disease. Those who had been inoculated 7 years before had the disease in only a moderate degree. A person who had been inoculated with Weigl's vaccine 7 months previously showed a certain degree of immunity. A favourable result, shortening of duration of illness, was obtained in one case by prophylaxis with convalescent serum. This was given in the first three incubation days in large doses. This shows the necessity for laboratory work to be carried out only by persons who have already been repeatedly protected by inoculation.

W. P. Kennedy.

STURM (Alexander). Das Fleckfieber und seine Bedeutung für die klinische Pathologie des Stammhirns. [**The Significance of the Clinical Pathology of the Brain-Stem in Typhus Fever.**]—*Klin. Woch.* 1942. Oct. 10. Vol. 21. No. 41. pp. 899–904. [54 refs.]

The greater part of this lengthy paper consists of an erudite discussion of the close association that exists between the clinical manifestations of typhus fever and lesions of the brain stem. The vasomotor disturbances such as tachycardia and low blood pressure, which are often followed in the later stages by bradycardia and high blood pressure, are attributed to damage of the vasomotor centres of the mid-brain. Bronchopneumonia, gastro-intestinal disturbances, hypocalcaemia, hypochloraemia, deviation to the left of the leucocyte index, nephritis, polyuria, hyperthyroidism, insomnia, motor disturbances, etc., are all believed to result from a destructive proliferative thromboangeitis which interferes with the blood supply of the various centres of the brain stem, especially those of the hypothalamus.

The author's personal experience of the differential diagnostic features in the early stages of the disease are interesting. Special stress is laid on the following points—(1) The rapid, or even sudden, onset simulating influenza, with fever, pains in the head and limbs, (2) pronounced insomnia, (3) a strikingly dry, often leathery, tongue

such as is not seen in the early stages of other infections (though the author states that other observers have described the tongue as being frequently moist), (4) a specially pronounced deviation to the left of the polymorphonuclear index, (5) a moderate acceleration of the sedimentation rate of the erythrocytes in contrast with the great reduction that occurs in central pneumonia, and (6) an early positive diazo reaction is often seen.

The rash is not a reliable guide; it was typical in only 10 of the author's cases, but the total number is not stated. In 3 cases it was completely absent, though one of these was fatal and another severe. The Weil-Felix reaction may give equivocal results; sometimes the titre was only 1–50 on the 10th day in severe cases and titres of 1–200 occurred in some cases that were not typhus. At the same time the great value of the test in diagnosis is fully recognized.

John W. D. Megaw.

WENSCHR. **Neurological Contribution to the Clinical Picture of Typhus.** —*Deut. Med. Woch.* 1942. Oct. 2. Vol. 68. No. 40. p. 984.

The diagnosis of typhus can be facilitated in the early stages by neurological signs. The first indication is sudden high rise in temperature accompanied by a quite typical and unusually stubborn headache which responds only slightly to analgesics. An additional sign is hardness of hearing which occurs in almost all cases. If these signs are accompanied by speech disorders and the characteristic twitching of the perioral muscles, the diagnosis of typhus exanthematicus is assured even without a distinct exanthem.

Therapy consists in relieving the pressure. Apathy or restlessness respond quickly to lumbar puncture, circulation and respiration definitely improve and the distressing headache disappears. Along with the essential care which must be paid to the cardio-vascular system, the main therapeutic concern is the prompt reduction of increasing pressure in the c.s.f. For this reason strophanthin should always be given in strongly concentrated glucose solutions which exert a dehydrating action. After damage to the vasomotor and respiratory centres, the next most important danger is the occurrence of bulbar paralysis. Recovery from the other nervous symptoms which may appear is usual, and they do not endanger life.

W. P. Kennedy.

LEON (Alberto P.). Precipitación de sueros anti-tifo por la orina de enfermos de tifo exantematico. Una nueva reacción serologica para el diagnostico del tifo. [**The Precipitation of Anti-Typhus Serum by the Urine of Typhus Patients. A New Serological Test for Typhus Fever.**]—*Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1942. Sept. Vol. 3. No. 3. pp. 201–208.

Two tests are described; one is new and the other is a modification of the "collodion fixation" reaction of K. Goodner (1941) [reference incomplete]. The new test is called the "precipitation reaction." The patient's urine is poured into a narrow test tube, to this is added, very slowly to prevent mixing, an equal quantity of a mixture consisting of one part of anti-typhus serum and four parts of an 8·5 per cent. solution of sodium chloride. A positive result is shown by the appearance, within one or two hours, of a disk of precipitation at the junction of the two fluids. Normal urine is used as a control. Of 29 tests made

on typhus patients 13 gave positive and 16 negative results. Urine diluted 1–10 was also tried: with this the positives appear to have been five and the negatives 12.

In the Goodner fixation test urine in various dilutions is added to diluted anti-typhus serum freshly mixed with a solution of "mucina granular" (Type 1701 W., of the Wilson Laboratory, Chicago). After thorough shaking the mixture is kept for an hour or two at room temperature and for 12 hours in a refrigerator. The tubes are centrifuged for five minutes at 500 to 1,000 revolutions a minute and then gently shaken. The reaction is read in terms of "+ to +++ of agglutination." With single specimens of urine of typhus patients the positives are said to be 63 per cent.; with 24–hour specimens 80 per cent. This reaction is likely to appeal only to research workers, who must consult the original paper for details of the technique.

The claim is made that in some cases the diagnosis can be made earlier than by the Weil-Felix test, but the "precipitation" test was carried out in only two cases before the fifth day, and one of these gave a negative result. The "fixation" test was positive in four cases and negative in one before the fifth day, but the technique is rather complicated and "anti-typhus serum," human or rabbit, cannot be regarded as a standardized reagent. *John W. D. Megaw.*

TRAUTMANN. Frühzeitige, objektive Prognosenstellung bei Typhus exanthematicus mit Hilfe des Weltmannschen Koagulationsbandes. [**Early Objective Prognosis in Exanthematic Typhus by Weltmann's Coagulation Test.**]—*Deut. Med. Woch.* 1942. Oct. 23. Vol. 68. No. 43. pp. 1053–1055. With 3 figs.

Weltmann's little-known coagulation test (WSK) as modified by TEUFEL is based on the observation that varying quantities of 0·5 per cent. solution of calcium chloride have to be added to 5 cc. of 1 in 50 dilutions of patients' sera in distilled water before coagulation of albumin occurs on boiling the mixture.

The calcium chloride solution is added to the diluted serum in a test tube, two drops at a time; the mixture is shaken and boiled after each addition and the reading is recorded in terms of the number of additions that have to be made before coagulation occurs on boiling. If only two drops are needed the result is stated as WSK=10; if four drops, as WSK=9; if six drops, as WSK=8, and so on till 20 drops indicate WSK=1. With normal blood the reading is WSK 6½.

In 73 cases of typhus fever tested before the 15th day the following results were observed:—WSK=7 in 16 cases, all of which were mild; WSK=6 in 25 cases of which 13 were mild and 12 moderately severe; WSK=5 or less in 33 cases, all of which were severe. In all the eight cases with readings of WSK=3 or less death occurred.

The chart shows no significant differences in the titres recorded at varying stages of the fever but the index is said to rise to normal in convalescence and a decided fall is regarded as indicating a bad prognosis.

It is claimed that the test gives a clear indication of the prognosis even in the first few days of the disease and that it is decidedly helpful in differential diagnosis.

[This test has been used as an index of prognosis in pulmonary tuberculosis, see *Bulletin of Hygiene*, 1942, Vol. 17, p. 764.]

John W. D. Megaw.

LYDTIN. **Experiences with Typhus.**—*Muench. Med. Woch.* 1943. Jan. 1. Vol. 90. No. 1. p. 1.

The following is a translation of a German abstract of the paper dealt with :—

Early diagnosis of typhus is difficult and the laboratory reactions are unreliable in the early stages, although they will give 90 per cent. positive values in a later stage. The most certain early sign is splenic enlargement. Weil Felix values below a titre of 1 : 200 prove nothing. The author does not advise energetic measures to support the circulation except when the patients must be transported long distances. Sulphonamide and atebrin-plasmoquine treatment were quite valueless and in neither case was there any reduction of mortality. Encouraging results were obtained by the use of convalescent serum in early cases, and a definite reduction in mortality was obtained, but in the later stages the serum was inactive. The disease took the mildest course in vaccinated persons. *W. P. Kennedy.*

SMITH (Felix) & EVANS (R. Winston). **Murine Typhus in British Soldiers in West Africa.**—*Lancet.* 1943. Jan. 30. pp. 142–143.

Four cases of "endemic murine typhus" in British soldiers are reported from a West African Colony in which the disease has not hitherto been recorded. The clinical features and the Weil-Felix reactions point clearly to a fever of the typhus group, but there is no mention of the epidemiological and laboratory findings on which the diagnosis of murine typhus has been based. Three of the patients came "not only from the same billet but actually from the same bed, each case moving into the infected bed as the previous occupant left it to be admitted to hospital." The dates of onset of these three cases are not stated and there is no reference to a search for insect or rat infestation. The other patient, who was the first to be attacked, "could not well have been more severely ill and survived."

The titres of the agglutination reactions were as follows :—

Case	Day of disease	*Proteus OX19*	*Proteus OX2*	*Proteus OXK*
1	12	625	625	250
	24	1,260	840	250
	41	1,000	840	315
2	8	315	125	125
	13	1,260	125	415
3	9	125	50	50
	17	1,260	315	415
4	9	50	50	50
	15	250	125	250
	24	1,260	315	315

In 11 control cases of other diseases, malaria, bacillary dysentery, undulant fever, etc. (all in persons who had previously been inoculated with T.A.B. vaccine) the following maximum titres were observed :—

Titre	Nil	25	50	125	250	315	415
Proteus OX19 ...	1	1	8	1	—	—	—
Proteus OX2	—	—	5	4	2	—	—
Proteus OXK ...	—	1	2	2	3	2	1

John W. D. Megaw.

SORDELLI (A.), MANZULLO (A.), RIESEL (M. A.) & FERRARI (J.). Tifus exantemático I. La infección experimental de animales de laboratorio con la sangre de enfermos de tifus exantemático de Bs. Aires, Córdoba y Santa Fe. [**Experimental Infection of Laboratory Animals with the Blood of Typhus Patients from Buenos Aires, Córdoba and Santa Fe.**]—*Rev. Inst. Bacteriológ. "Dr. Carlos G. Malbran."* Buenos Aires. 1942. Dec. Vol. 11. No. 2. pp. 192–209. [10 refs.]

The experiments described in this paper were carried out for the purpose of isolating Rickettsiae from 13 patients suffering from clinical typhus fever. The disease was assumed to be of the murine type though the report does not deal with its clinical or epidemiological features. Sixteen guineapigs and one rat were inoculated by the intraperitoneal route, each animal received 3 to 4 cc. blood. Three to 12 passages were made in each case through guineapigs ; full doses of brain, spleen and suprarenal substance were inoculated ; when available, scrapings from the tunica vaginalis were also used. Scrotal reactions occurred in only six of the 86 guineapigs used, but never in the first two passages ; in one strain the positive reaction did not occur till the 11th passage. The febrile reactions lasted only one, two, or at most three, days, and even when scrotal reactions were seen the guineapigs of the preceding or subsequent passages often had " inapparent " infections. Rickettsiae were found in smears from the tunica scrapings of only two of the animals that had scrotal reactions. In the case in which a primary inoculation was made in a rat the response was slight ; a scrotal reaction occurred in the rat of the third passage and Rickettsiae were found in the scrapings ; inoculations into a series of rabbits with blood from the same patient gave negative results throughout. Blood corpuscles freed from serum by washing and centrifuging the citrated blood were used in some cases ; rats and guineapigs sensitized by irradiation with X-rays or by daily intraperitoneal inoculations with normal guineapig serum were often employed ; yet altogether it was possible to isolate Rickettsiae from only 6 of the 13 patients. Three of the positive results were in the nine patients in whom positive Weil-Felix reactions indicated the development of antibodies ; the other three were in four patients whose reactions were still negative.

Even the sensitized rats were little affected in health by the inoculations and none of them died. In spite of the use of scrapings rich in Rickettsiae, when these were available, it was never possible to establish a strain which gave regular febrile and orchitic reactions.

Although these results were much like those observed in certain laboratory strains of the historic virus the authors disclaim any intention of denying that the virus was of the murine type.

[The authors' disclaimer may possibly refer to the type of the disease rather than to that of the virus, which certainly was far from being typically murine. Although the authors admit that the conditions were not ideal for the investigation, this was much more thorough than is usually possible in cases of this kind. An epidemiological enquiry might yield interesting results.] *John W. D. Megaw.*

ANIGSTEIN (Ludwik) & BADER (Madero N.). **New Epidemiological Aspect of Spotted Fever in the Gulf Coast of Texas.**—*Science.* 1942. Oct. 16. Vol. 96. No. 2494. pp. 357–358.

Referring to a recent outbreak of spotted fever in Texas, from which strains of the infective agent were isolated and produced in guineapigs immunity to a Montana strain of Rocky Mountain spotted fever, but not to louse- or flea-borne strains of typhus Rickettsiae, the authors point out that the only tick found in a search of the locality in which the outbreak occurred was *Amblyomma americanum.* This tick is known to be an efficient carrier of the spotted fever Rickettsiae under experimental conditions [see this *Bulletin*, 1933, Vol. 30, p. 899] but has not been proved a vector in nature. Members of the genus Amblyomma, however, are known vectors in Brazil; the present experience suggests strongly that *A. americanum* is a vector in Texas. If this is so the Texas disease would resemble, epidemiologically, that of Brazil rather than that of the Rocky Mountains. *C. W.*

TRAVASSOS (J.) & VALLEJO (A.). Comportamento de alguns cavídeos (*Cavia aperea* y *Hydrochoerus capybara*) às inoculações experimentais do virus da febre maculosa. Possibilidade desses cavídeos representarem o papel de depositários transitórios do virus na natureza. [**The Response of Certain Caviidae** (*Cavia aperea* **and** *Hydrochaerus capybara*) **to Experimental Inoculation with the Virus of Spotted Fever. The Possibility that these Caviidae may be Natural Reservoirs of Infection.**]—*Mem. Inst. Butantan.* 1941. Vol. 15. pp. 73–86. With 5 graphs. [15 refs.] English summary.

The cavy locally known as "preá" and the capybara are common in the rural areas of São Paulo in which tick-borne "spotted fever" is prevalent. The authors have now proved that both of these rodents are susceptible to experimental inoculation with the Rickettsiae of the disease. The cavy reacts in the same way as the guineapig; the capybara is less severely attacked but harbours infection in a fully virulent form for at least eleven days.

Captured animals were used in the experiments and only small numbers were available. Some of the cavies and capybaras were found to be immune, presumably because of previous natural attacks of the disease. None of the captured animals was found to be harbouring the virus.

Ticks are believed to be lasting reservoirs of infection, which is known to be transmitted to their offspring: the rodents act as temporary reservoirs, they probably cause periodical increases in the virulence of the Rickettsiae and dissemination of the infected ticks. The severity

of the human disease is greatest in the places in which the rodents are most numerous; presumably because of the opportunities for rapid transmission of infection from animal to animal.

John W. D. Megaw.

TRAVASSOS (J.) & VALLEJO (A.). Possibilidade de *Amblyomma cajennense* se infetar em *Hydrochoerus capybara* experimentalmente inoculado com o virus da febre maculosa. [**Transmission of Infection by *Amblyomma cajennense* from *Hydrochaerus capybara* Experimentally Infected with the Virus of Spotted Fever.**]—*Mem. Inst. Butantan.* 1941. Vol. 15. pp. 87–90. With 1 graph. English summary (3 lines).

The authors have transmitted a laboratory strain of the Rickettsiae of spotted fever from an experimentally inoculated capybara to a guineapig by the bites of laboratory bred ticks (*Amblyomma cajennense*).

Two ticks from a clean batch were allowed to feed on an infected capybara but were not left on long enough to become fully engorged; they were kept for six days at laboratory temperature and then were fed for four days on a healthy guineapig, which in due course developed fever. On the tenth day of the attack the animal was killed and was found to have typical lesions, including great enlargement of the spleen. Rickettsiae were isolated from the guineapig. It was concluded that the capybara is one of the animal reservoirs of the tick-borne spotted fever of São Paulo.

John W. D. Megaw.

WERNER (H.). Zur Diagnose des Fünftagefiebers. [**The Diagnosis of Five-Day Fever (Trench Fever).**]—*Deut. Med. Woch.* 1942. Sept. 18. Vol. 68. No. 38. pp. 934–935.

This is a discussion in general terms of the possibilities of laboratory diagnosis of trench fever, which has again come into prominence as a war disease. The suggestions are based entirely on what was known of the disease before the outbreak of the present war, and on analogy with recent work on the Rickettsiae of the fevers of the typhus group.

One suggestion is to allow clean laboratory bred lice to feed on the patients during the febrile attacks and to examine the insects four or five days later. Abundant growth of Rickettsiae will be found in infected lice. The method of examination is not stated. The Rickettsiae will be seen in the lumen of the gut or round the epithelial cells, not inside the cells as is the case in typhus fever. The lice are applied in special cages and it must be remembered that they become infective for man after the fourth or fifth day.

Successful cultivation of the Rickettsiae in the testicles of rabbits has been carried out by OGATA, who has also transmitted the virus through rabbits by repeated transfers; the rabbits of the early passages give no apparent response but in the later passages the testicles yield an abundant growth of Rickettsiae.

LEDINGHAM and ARKWRIGHT in the 1914–18 war used suspensions of the Rickettsiae from the guts of infected lice for agglutination tests which appear to have given specific responses. Cultures in the yolk sacs of developing chick embryos may possibly be suitable but these are not yet available. The author, surprisingly, refers to OTTO and GILDEMEISTER in connexion with the use of yolk-sac cultures of Rickettsiae for protective inoculation against typhus, and does not mention the name of COX.

John W. D. Megaw.

SMITH (D. J. W.). **Studies in the Epidemiology of Q Fever. 10. The Transmission of Q Fever by the Tick *Ixodes holocyclus* (with Notes on Tick-Paralysis in Bandicoots).**—*Australian Jl. Experim. Biol. & Med. Sci.* 1942. Sept. Vol. 20. Pt. 3. pp. 213–217.

The "scrub-tick," *Ixodes holocyclus*, is the tick that most commonly attacks man in Australia; it has now been shown to be a potential vector of Q fever. An adult *I. holocyclus*, previously infected experimentally in the nymph stage by feeding on an infected bandicoot, transmitted the disease to another bandicoot on which it fed.

Nineteen male and 29 female ticks were fed on an infected bandicoot; of these, nine females became infected; in the rest no Rickettsiae could be detected. The Rickettsiae were passed from larval ticks to nymphs and from nymphs to adults, but not to any of the numerous progeny of three infected ticks.

No infection was found in 109 nymphal and adult ticks collected from 28 bandicoots trapped in the coastal district north of Brisbane and inoculated into 23 guineapigs; 111 larval ticks were also uninfected. An experiment mentioned by the author suggests that bandicoots soon cease to be infective to ticks; 25 nymphs removed from a bandicoot, from which a strain of *Rickettsia burnati* was isolated, failed to infect a guineapig into which they were inoculated: in this case the bandicoot was still infected while the ticks were feeding on it but was no longer infective to them.

The author considers that the tick may transmit infection to man in two ways, either by infecting domestic animals from which persons become infected, or directly by its bite. *John W. D. Megaw.*

YELLOW FEVER.

BUSTAMANTE (Miguel E.). Distribución geografica de la fiebre amarilla en Mexico de 1800 a 1923. [**The Geographical Distribution of Yellow Fever in Mexico between 1800 and 1923.**]—*Rev. Inst. Salubridad y Enfermedades Trop. Mexico.* 1942. June. Vol. 3. No. 2. pp. 93–105. With 1 map. English summary.

The last case of clinically typical yellow fever in Mexico was reported in January 1923, but protection tests show that cases had occurred at least till 1925. In the last epidemic of 1919–23 the States of Tamaulipas, Veracruz and Yucatán on the coast of the Gulf of Mexico, and Sinaloa and Jalisco on the Pacific coast were attacked epidemically; in other States, Tabasco, Campeche and Quintana Roo on the Gulf of Mexico and Sonora, Colima and Oaxaca on the Pacific coast reported sporadic cases. For example, Veracruz had 598 cases, 343 deaths, Yucatán 72 cases, 30 deaths, Sinaloa 107 cases, 71 deaths, whereas Campeche had 2 cases, one fatal, Quintana Roo 3, all fatal, Colima 7 cases, 4 deaths, Oaxaca 3, all fatal. [The second table setting forth some of these points contains several errors.] It is thought, therefore, that the jungle form exists in these areas of sporadic cases. Drs. KUMM of the Rockefeller Foundation, HERRERA of Guatemala, and BUSTAMANTE of Mexico, took 807 samples of blood from persons in the Usamacinta Valley, from Petén, Guatemala, to Chiapas and Tabasco, Mexico, in April and May 1942 and sent them to the Yellow Fever

Laboratory, New York. The results of examination of these will be recorded later. This area was selected because it has been a "silent region" while epidemics were raging elsewhere in the neighbourhood. A list of outbreaks of yellow fever in Mexico between 1800 and 1923 is given and a map showing 127 places where these outbreaks took place.

H. Harold Scott.

FINDLAY (G. M.). **The Action of Certain Surface-Acting Substances on Yellow Fever Virus Neurotropic Strain : Preliminary Observations.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1943. Jan. 30. Vol. 36. No. 4. pp. 247–252.

Attempts to produce immunity with yellow fever virus inactivated by heat, ultra-violet light or formaldehyde have been unsuccessful. The present work was undertaken to find out if certain surface-acting substances would inactivate the virus and yet permit it to retain its antigenic properties.

The brains of mice infected with this virus were ground up in serum saline (1 in 10) to make a 20 per cent. suspension : this suspension was then mixed with an equal quantity of the substance to be tested for its power of inactivation. The final concentrations of each compound in the mixed suspension were 0·1, 0·2, 0·4, 1·0 and 2·0 per cent. and the *p*H was adjusted to 7·0–7·2 by means of phosphate buffer. The mixtures were kept at 37°C. for two hours and then injected intraperitoneally into mice which, immediately before, had received intracerebrally 0·03 cc. of a 2 per cent. suspension of starch in saline. In all, 37 substances were tested and the results are given in tabular form.

A large number of agents were found capable of inactivating the virus, but their chemical constitution revealed no general law by which it was possible to determine whether a substance would cause inactivation. Sodium oleate, linoleic and linolenic acids were all active inhibiters, thus bringing their action on yellow fever virus into line with that on various other viruses such as Rous sarcoma, vaccinia, influenza A, etc.

The number of substances which allowed the persistence of some degree of the antigenic properties of the virus was much smaller than that which had produced inactivation, and included acetyl-salicylic acid, linoleic, linolenic, maleic and mucic acids and tetralene.

Virus treated with these substances induced immunity in a proportion of the mice.

E. Hindle.

PLAGUE.

MOLL (Arístides A.) & O'LEARY (Shirley). **Plague in the Americas. XII. The West Indies and Certain European-African Islands.**—*Bol. Oficina Sanitaria Panamericana.* 1942. Oct. Vol. 21. No. 10. pp. 980–1000. With 2 maps & 1 chart. [Refs. in footnotes.]

In this study the survey of plague in the Americas has been transferred from the Mainland to the West Indian Islands. The history of

plague in these islands might suggest an immunity or resistance of tropical islands to plague, were it not for the similar "immunity" enjoyed by other non-insular regions in America and for the persistence of the disease in similarly-situated islands in other parts of the world. The West Indian islands dealt with are Barbados, Cuba, Grenada, Jamaica, Porto Rico and the Virgin Islands. Some discussion is also devoted to the Azores, Canary and Cape Verde Islands of the European and African zones. Neither Barbados nor Jamaica has reported human plague and although Jamaica was visited in 1912 by a ship with plague rats on board this was discovered and the fumigation adopted seems to "have prevented an invasion of the island." [The discovery of the plague-infected rats was made by Dr. (now Sir Harold) SCOTT (lately Director of the Bureau of Hygiene and Tropical Diseases), who took steps to prevent the sailing of the ship a few hours before she was due to leave.] The dates of record of plague for the islands were :—Cuba 1912, Grenada 1912, Puerto Rico 1912, Trinidad 1907, Virgin Islands 1908, Azores 1908, Canary Islands 1906, and the Cape Verde Islands 1921. Much the same antiplague measures were adopted as in other places. *W. F. Harvey.*

DEVIGNAT (R.). L'aeration des milieux liquides de culture par barbotage d'air. [**Aeration of Liquid Media.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 145–160. With 1 fig. and 1 chart. [Summary appears also in *Bulletin of Hygiene.*]

The principle of continuous aeration of the incubating culture is the same as that of the aquarium tank. It may, in fact, be very conveniently accomplished by means of an electromagnetic pump. The author has worked out in very complete detail a method which makes use of comparatively simple apparatus to bubble air continuously through the culture. This air is washed by passing through an alkaline solution which disembarrasses it of its content of carbonic acid, and so prevents acidification of the medium. A clear line-drawing, with lettering, gives all the detail that is necessary to understand the setting up of the apparatus. The method is not new and the author found that it had already been used by TOPLEY and WILSON for the very purpose of restoring the oxygen necessary for bacterial growth to culture media after autoclaving. Otherwise air could only return to the inoculated medium in the incubator by the slow method of absorption and diffusion. The increase of growth obtained in the aerated over the non-aerated culture varies somewhat for different organisms. In bouillon of *p*H 6·7 to 7 after 48 hours' incubation it was three to five times as great for the plague bacillus, six times for the typhoid bacillus, and eight times for the anthrax bacillus. In bouillon of *p*H 7·5 it was found that the growth after 48 hours was 10 times, 9 times and 15 times greater than the control for paratyphoid A, Shiga and typhoid bacilli respectively, while *Brucella melitensis* grew 20 times more abundantly in three days. Another great advantage of the continuous agitation by bubbles of air was that the culture suspensions remain uniform without formation of clumps or chains, which renders them extremely useful for agglutination reactions. The author considers that the prime factor in increasing the growth is oxygenation and not the mechanical agitation of the culture. *W. F. Harvey.*

DEVIGNAT (R.) & SCHOETTER (M.). Le bacille de Yersin en milieu aéré. [**The Plague Bacillus in Aerated Medium.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 161–181.

A special study of the effects of continuous aeration during incubation on the plague bacillus has been made by the authors. In the first place it was shown that this elaboration of the technique of culture did not entail any greater risk of contamination. Other points investigated had reference to changes in morphology, the agglutinability of aerated cultures and, most important of all, the rapid loss of virulence of a strain brought about by aeration. Morphological changes of size were observed in the aerated cultures and there was a great tendency for the bacilli to remain isolated. The main change, however, observed in those organisms on their way to loss of virulence by aeration was vacuolation. Aeration will serve to prepare agglutinable suspensions of the plague bacillus, but their agglutinability is inferior to that of the suspension of an agar culture in normal salt solution.

It was found in the course of experimentation that after several passages in aerated medium at 37°C. two highly virulent local strains had lost their virulence after 30 to 36 days of this treatment. The rapidity of attainment of this result may be contrasted with that for the well-known E.V. strain, which, incubated at 16–20°C., required subculture monthly for five years to deprive it of its virulence. The Javan strain Tjiwidej, on the other hand, became avirulent in six months. In the latter case the principle of dissociation was adopted with selection of avirulent colonies.

Great importance is attached to the preservation of antigenic power by avirulent strains. The two characters do not necessarily go together. It was found by the authors that their strains, which they had rendered avirulent by aeration, preserved a high degree of antigenic power—one which was quite comparable, in the guineapig, with the well-established antigenic potency of the E.V. vaccine. *W. F. Harvey.*

VINCKE (I.) & JANSSENS (P. G.). Etude expérimentale comparée d'immunisation antipesteuse par germes vivants atténués et par la lymphe de Haffkine. [**Experimental Study of the Relative Merits of Anti-Plague Immunization by Living Attenuated and Dead Vaccine.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 86–103. [14 refs.]

Most of the main facts and contentions regarding the prophylactic use for immunization of living or dead plague vaccines are now well known. The present authors have experimented with a local virulent strain of plague to test the degree of immunity conferred on guineapigs by the rival vaccines. Three of these freshly isolated Lake Albert strains were tried out, one obtained from man, one from Ctenocephalus and one from Sarcopsylla. All three killed the guineapigs (75) without exception in dilutions ranging from 1–1,000 to 1–10,000,000, in a dose of 0·5 cc. The human strain 2,831 was chosen for the immunity testing Full details of the several experiments are available and the general conclusions drawn give the substance of the authors' work. These were :—

(1) The strains, 2,831 of human origin, 2,846 from Ctenocephalus and 2,849 from Sarcopsylla isolated in the endemic plague zone of Lake Albert, killing the guineapig in doses of 5 to 20 organisms, can be

considered as highly virulent and satisfying the conditions of infection experiments. (2) The avirulent plague strain E.V. of GIRARD, maintained for 12 months in the Belgian Congo, had retained its characters of avirulence and immunizing power. (3) The laboratory guineapig stock proved uniformly sensitive to plague bacilli. (4) The strain E.V. confers immunity in 97 per cent. of cases on guineapigs, in doses varying from 2,000 million to 1,000 organisms, to the inoculation of a standard lethal dose of a very virulent local plague strain. (5) Haffkine's vaccine in doses varying from 5,000 million to 1,000 organisms only immunizes the guineapig in 12·5 per cent. of cases with the same infecting dose. (6) The advantage of vaccination by avirulent living organisms would appear to be such as to justify its current use, in spite of difficulties of a local nature. The remark is made subsequent to the conclusions that since 1938 several thousands of vaccinations with living avirulent organisms have been performed in man without difficulty or inconvenience. *W. F. Harvey.*

CHOLERA.

GORDON (J.) & GORDON (M.). **Involution Forms of the Genus Vibrio Produced by Glycine.**—*Jl. Path. & Bact.* 1943. Jan. Vol. 55. No. 1. pp. 63–68. With 2 figs. on 1 plate.

Glycine had previously been found, when added to nutrient media, to produce striking morphological changes in organisms of the coli-typhoid group. Their colonies were sticky and tenacious, suspension in water was difficult, and the organisms became enlarged and swollen. Completely normal characters were restored by transference to ordinary nutrient agar. Similar degenerative changes have been brought about in other organisms, especially in those of the cholera group which forms the subject of the present study. Experiments were instituted also to determine whether similar effects could be produced by substances having a lethal effect on cholera organisms and whether these and other substances might inhibit the glycine effect. The results of these experiments may be summarized: (1) Glycine in concentrations from 0·5 to 1·5 per cent. produces stickiness of colonies and causes swelling of the organisms to spherical or oval bodies. (2) Glucose produces cocco-bacillary involution forms of its own and prevents the changes produced by glycine. (3) "Various substances in concentrations which have a marked inhibitory effect on growth—carbolic acid, *p*-aminobenzoic acid and α-aminomethanesulphonic acid—added to glycine agar prevent the formation of these involution forms." Their action may possibly be to interfere with the utilization of the glycine. (4) Alanine in high concentration produces a somewhat similar effect to glycine. *W. F. Harvey.*

REICHS-GESUNDHEITSBLATT. 1941. Aug. 20. Vol. 16. No. 34. pp. 615–619.—Cholera-Merkblatt. [**Memorandum on Cholera.**]

This publication is exactly what it is entitled and is a plain, practical account of what the medical officer and the public authority should know and do in the presence of, or on the appearance of, cholera or cholera-suspected cases. It is a public health leaflet and could be

purchased singly or in packets from the Public Health Department. It is essentially text-book "Applied Tropical Medicine." There are 16 headings, which it is interesting to set out: (1) Cause and Nature of Cholera; (2) Notification and Regulations; (3) Transmission of the Disease; (4) Prevention; (5) Course; (6) Treatment; (7) Segregation, Procedure, and Care of the Patient; (8) Rules for Attendants; (9) Treatment of Excreta, Food and Drink Residues; (10) Laundry, Clothes and Objects of Use; (11) Bacillus Carriers; (12) Disinfection of Dwellings; (13) Food Trading; (14) Conveyance of Cholera Patients; (15) Treatment of Cholera Bodies; (16) Disinfectants.

Notification of cholera or suspected cholera is incumbent on: (1) the doctor, (2) the head of the household, (3) anyone having dealings with the patient, (4) anyone in whose house a case of, a suspected case of, or a death from cholera has occurred. Inoculation with killed cholera vaccine is recommended prophylactically: 2 to 3 inoculations at intervals of 5 to 10 days. The protection afforded should last 6 to 9 months and vaccination should then be repeated. Disinfectants recommended are: cresol (2·5 per cent.), quicklime, chlorinated lime and formalin. *W. F. Harvey.*

BACILLARY DYSENTERY.

WALTHER (G.). Ueber Azotämie bei Flexnerruhr. [**Azotaemia in Flexner Dysentery.**]—*Klin. Woch.* 1942. Nov. 7. Vol. 21. No. 45. pp. 988–991.

This paper gives the results of blood chemical analyses in 49 cases of moderate and severe Flexner dysentery seen in the Russian campaign in 1941.

Methods.—For "Rest N" estimation the serum proteins were precipitated with 1·55 per cent. uranium acetate solution; for non-protein nitrogen the serum protein precipitant was 5 per cent. trichloracetic acid; the nitrogen content of the filtrates was estimated by ashing and Nesslerization.

[Rest nitrogen is "total non-protein nitrogen" plus nitrogen derived from "diamino acids and high molecular weight polypeptides."]

The total volume of circulating plasma was indirectly deduced from its protein concentration, on the assumption that the total weight of circulating protein remained roughly constant, and therefore that increase in concentration of protein in the plasma indicated reduction in circulating volume, *i.e.* if the plasma protein concentration was found to be twice normal, the total plasma volume was assumed to be halved [this is very doubtful, and, incidentally, the figures give the surprising result that the milder cases of dysentery had very low plasma volumes, whereas the severe cases had volumes approaching normal. The derived figures for "total circulating rest N" are therefore of little value.]

Results.—Concentrations of rest N were found from 43 to 120 milligrammes per 100 cc. (normal 20–40).

On the whole the severer cases had the higher concentrations, which dropped towards normal as the patients recovered from the dysentery. No close relation was found between rest N and Na or chloride concentrations in the plasma.

There was a striking drop in "Difference N" concentration (*i.e.* rest N minus non-protein N) as the patients recovered.

No tests were performed to assess renal function.

Nitrogen retention in severe diarrhoea is well known and probably has more than one cause, namely, haemo-concentration due to water loss, increased protein breakdown in a severe infective disease, renal failure due to toxic effects on kidney parenchyma.

[No mention is made of the possibility of renal failure due to diminished volume of circulating blood; this paper throws no new light on the cause of nitrogen retention in severe diarrhoea.]

H. K. Goadby.

WILSON (D. C.). **Notes on the Treatment of Bacillary Dysentery.**—*Jl. Roy. Nav. Med. Serv.* 1942. Oct. Vol. 28. No. 4. pp. 357–361.

This is a clinical study, the result of two years' observation in the Middle East.

Diagnosis.—In addition to the text-book symptoms an almost constant diagnostic sign was tenderness over the descending colon in 95 per cent., and as diminution in pain coincided with improvement in the general condition it served as a useful indication in treatment. Diagnosis should be made provisionally on physical signs together with cytodiagnosis of stools, and treatment instituted without delay. Blood slides should be examined immediately to exclude the possibility of subtertian malaria.

Treatment.—Cases are divided into mild, moderate and severe, which roughly corresponded to *Bact. schmitz* or *sonnei* (mild), *flexneri* (moderate) and *shigae* (severe). In all types of less than three days' duration treatment was initiated with a dose of half an ounce of castor oil, and the patient was kept on water only, in ample quantities. Sodium sulphate was employed in mild cases only as no advantage is to be gained by further dehydrating an already dehydrated patient. Kaolin in doses of 2 drachms thrice daily should be employed once the stools have become faecal, and recovery should be complete by the 10th day. Moderate cases, even when the infection is due to *Bact. shigae*, responded quickly and satisfactorily to sulphaguanidine. The results with this drug, compared with the previous treatment with sodium sulphate, were startling. The average time of recovery was reduced from 10–16 to 7 days.

The dosage of sulphaguanidine was 0·1 gm. per kilo. as initial dose, followed by 0·05 gm. per kilo. every four hours till the number of stools fell to five in 24 hours; thereafter 0·05 gm. per kilo. eight-hourly.

In practice it was found that 60–90 gm. were given in three or four days in moderate cases. In no case was any reaction or drug toxaemia observed.

Sulphonamide [*sic*] was tried out in a series of moderate cases, but in order to obtain results it was necessary to keep concentration high by giving an initial dose of 2 gm. followed by 1 gm. every two hours for 24 hours, then 1 gm. four-hourly for a further period of the same duration, by which time signs of toxaemia have set in. The results were on the whole good, but in a few cases sulphaguanidine had to be substituted owing to lack of response.

The severe cases were medical emergencies and were put on sulphaguanidine as soon as possible, and 40,000 units of *shiga* anti-dysenteric serum were injected intramuscularly. Dehydration was treated by

drip transfusion, 5 per cent. glucose in normal saline up to 10 pints, if necessary, but when stool culture was positive for *Bact. shigae* and the condition of the patient indicated it, anti-serum up to 100,000 units was added to the drip.

Cases with commencing peripheral vascular failure with blood-pressure below 100 mm. were given a pint of plasma in addition. Good nursing is most important and sister and ward staff should be experienced in the management of dysentery. Patients should be encouraged to drink large quantities of fluid, and the provision of suitable diet in all stages is important. Stout is the most useful tonic in convalescence. Since the advent of sulphaguanidine the occurrence of complications has diminished.

Pain, colicky or continuous, is relieved by tinct opii, 15 min. at night. This has the added advantage of slowing peristalsis, and thus permitting greater concentration and more prolonged action of sulphaguanidine. Haemorrhage was very serious in five cases, but appendicostomy, to relieve tension in the large intestine, proved entirely successful. In the sixth it was only partially so, so that transverse colostomy was performed and resulted in stopping further blood loss; subsequently the colostomy was closed.

Hiccough appeared to be due to deep ulceration into the muscular coat giving rise to peritoneal irritation, and was invariably a symptom of great gravity. In three fatal cases perforation occurred. All cases of arthritis eventually recovered though no specific treatment appears to hasten recovery.

Twenty cases with controls were treated with bacteriophage supplied by Dr. Compton, but the results were variable and disappointing as compared with those obtained with sulphaguanidine.

In a period of two years over 3,000 cases were admitted as possible dysenteries, of which 1,978 were bacteriologically positive. There were seven deaths, giving a case mortality of 3·5 per thousand, the causes being: perforation of the large intestine 3, peripheral vascular failure 1, toxaemia 2, pneumonia 1. *P. Manson-Bahr.*

Bulmer (Ernest) & Priest (W. M.). **Sulfaguanidine in the Treatment of Bacillary Dysentery.**—*Jl. Roy. Army Med. Corps.* 1942. Dec. Vol. 79. No. 6. pp. 277–286. With 1 chart.

During 1941, out of 2,066 soldiers treated for acute diarrhoeal diseases in the Middle East, more than one-quarter (554) were suffering from bacillary dysentery; 76 patients were treated with sulphaguanidine and there were two deaths. The use of the drug was restricted to carefully selected patients, who comprised 13 per cent. of the whole. Patients received nothing but water for the first 12 hours. Salines were withheld on the grounds that purgation of an already dehydrated patient was undesirable. In very acute cases blood and plasma transfusions have been given with marked benefit.

There were few grave cases in the series and complications were almost absent. On the whole the disease has been mild or moderate in severity and there has been a tendency to chronicity.

Complications were rare, there was one case of arthritis and one of benign haemorrhagic nephritis unaccompanied by oedema or nitrogen retention; this patient recovered in three days.

Standard doses of sulphaguanidine were adopted, as the drug was found to be entirely non-toxic. An initial dose of 6 gm. was given

and thereafter the drug was continued in doses of 3 gm. four-hourly until faecal porridgy stools were passed and general clinical improvement had been maintained for two or three days; then 3 gm. thrice daily for three or more days. The total quantity varied from 18 gm. to as much as 350 gm.; the average effective dose was not less than 50 gm. but was usually between 100 and 200 gm.

There were 54 acute and 15 chronic cases. Both the patients who died were in a critical condition on admission. One had a large pericolonic abscess. There were three failures, but these eventually recovered in spite of apparent non-response to sulphaguanidine. One had a severe Sonne infection which eventually recovered after rectal instillation of sulphonamide.

The authors regard general impressions as of greater value than any figures. The effects of sulphaguanidine may be judged by a change in the patient's general condition and improvement in stools. A notable diminution in temperature, pain and toxaemia took place within 24 hours; this was frequently dramatic and was fully appreciated by the patient. The change in the character of the stools is most impressive. In most cases they become porridgy and faecal within 48 hours; nothing comparable has been seen in saline-treated cases.

The authors conclude that sulphaguanidine appears to be as specific against dysentery bacilli as sulphapyridine is against the pneumococcus.

P. Manson-Bahr.

POTH (Edgar J.), CHENOWETH (Beach M.), Jr. & KNOTTS (F. Louis). **A Preliminary Report on the Treatment of Bacillary Dysentery with Succinyl Sulfathiazole.**—*Jl. Lab. & Clin. Med.* 1942. Nov. Vol. 28. No. 2. pp. 162–167. [16 refs.]

Experimental and clinical foundation for the use of succinyl sulphathiazole in the treatment of bacillary dysentery has already been laid by the two senior authors. They demonstrated that this drug had a much greater local activity against coliform organisms in the bowel than sulphathiazole and sulphaguanidine. It is claimed that the character of the faeces is profoundly altered by the action of succinyl sulphathiazole and that they become practically odourless.

The toxicity of this drug is unusually low and approximately 5 per cent. of the ingested compound is excreted by the kidneys when diarrhoea is absent.

The customary general symptomatic treatment was given to all patients, including the administration of adequate perenteral fluids. The diagnosis of bacillary dysentery was confirmed bacteriologically in all cases. The drug was given by the mouth and the dosage varied from 0·2 gm. to 1·0 gm. per kilo. daily, divided into six equal portions; the length of treatment was from two to seventeen days. There were no failures or deaths and the patients ranged in age from eight weeks to 83 years.

The response of ten children and infants when treated with succinyl sulphathiazole was prompt, whether treatment was begun early or late in the disease and it appears to be equally good with smaller as with larger doses. The temperature returned to normal in twenty-four hours or less in all instances, save one. The results of treatment of ten adults with succinyl sulphathiazole were equally good. The dosage was 0·25 gm. to 0·5 gm. per kilo. daily over a period from 4–17 days. [The doses given in this paper seem to be exceedingly high.]

The number of patients in this series was insufficient to determine accurately the minimum dosage of the drug and the shortest period of therapy required for the successful treatment with this drug. It appears that in most instances larger quantities were given, and for longer periods, than was necessary.

Bacteriological studies showed that Shiga's bacillus is especially susceptible to succinyl sulphathiazole. Dysentery bacilli disappear from the stools within 48 hours. The authors consider that it is significant that the response is immediate, even when the disease has been present for as long as three months before treatment is undertaken. It is emphasized that treatment of bacillary dysentery in the United States is specially favoured by the excellent nutrition of the majority of patients. *P. Manson-Bahr.*

LEPROSY.

British Empire Leprosy Relief Association (Madras Provincial Council). **Annual Report 1941–42** [Austin (T.), Chairman, Executive Committee].—26 pp. Chingleput: Printed at the Arpudha Press.

Much of the more important work summarized in this report has been already published and some is of local interest only. The following points are noteworthy. Special attention has been paid by Dr. R. G. Cochrane to leprosy in childhood and a children's Leprosy Sanatorium has now been opened in the Salem district with 25 residents and an out-patient clinic. Some success has been obtained with the plan of inducing infective patients in villages to attend for night segregation with a view to limiting contact infections arising from them, but it is too soon to estimate its value. The headquarters of the Madras work is at the Lady Willingdon Leprosy Sanatorium where much clinical research is being carried out. Epidemiological studies indicate that if the child rate is higher than that of adults the disease is probably spreading. House and family contact is by far the most important factor in relation to severe infections among children. No instance of early simple macular cases becoming bacteriologically positive have been met with. Lepromin tests gave very similar results to those reported from Calcutta. *L. Rogers.*

Degotte (J.). Application pratique des troubles de la sudation à l'établissement de l'observation clinique des lépreux. [**Investigation of Sweating Dysfunction in the Diagnosis of Leprosy.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 135–136. With 1 plate.

The author points out that in the Belgian Congo the prophylaxis of leprosy largely depends on early treatment in the macular stage, in the diagnosis of which he finds alteration in sweating to be the most frequent and objective diagnostic sign. To detect and measure this sign he injects pilocarpine to induce sweating, followed by swabbing the surface with an alcoholic solution of iodine and then powdering it with starch to produce blue points at the sites of the sweat glands. In order to be able to preserve records of the changes in the functions

of the sweat glands he made use of the fact that sweat contains a notable amount of chlorides, which react with silver nitrate to form silver chloride, which quickly becomes black on exposure to light. He therefore covered transparent paper with 5 per cent. silver nitrate in 4 per cent. gelatine and applied it to the sweating surface to bring out the activity of the sweat glands, and he preserved the negatives by treating them for a few seconds in a bath of paraffin at 100°–110°.

L. Rogers.

HELMINTHIASIS.

DORMER (B. A.). **A Preliminary Survey of Bilharzia in Native Schools in River Valleys on the Natal Coast.**—*South African Med. Jl.* 1942. Oct. 10. Vol. 16. No. 19. pp. 353–354. With 1 map.

The author surveyed the area (of which a sketch map is given) between the Tugela and Umkomaas Valleys and up to 25 miles inland from these. Only 18 days were allowed for the survey, so that one or at most two schools in each river valley were chosen (out of 119 schools in the whole area). Each child in these schools was asked whether blood was passed in the urine. No reliance was placed on replies stating that blood had been passed formerly.

Eggs of *Schistosoma haematobium* were found in the uncentrifuged deposit of the urine of 99 per cent. of children showing haematuria at the time of the examination; centrifuged specimens were also examined. In most of the schools some children were passing blood in the stools. In one of these eggs of *S. mansoni* were found and in one eggs of *S. haematobium*; others contained eggs of Ascaris, hookworms, and Trichuris and cysts of *Entamoeba histolytica* and *E. coli*.

All children passing blood in their stools were examined "in a general way" for undernourishment, but exact weights, heights, etc. were not noted. A clinical impression of vitamin deficiency was obtained from the appearance of the skin, eyes, lips, naso-labial folds, teeth and gums.

Of the 4,489 children examined, active urinary bilharzia was found in 10 per cent. The minimum was 0·87 per cent. in one of the Umvoti Valley schools and the maximum 39·61 per cent. in the Umkomaas Valley school. Further and more exact surveys are planned.

G. Lapage.

GELFAND (M.). **The Clinical Features of Intestinal Bilharziasis** (*S. mansoni*).—*Clin. Proc.* Cape Town. 1942. Aug. Vol. 1. No. 8. pp. 247–252.

Bilharzia is the commonest disease next to malaria in Southern Rhodesia; it causes many deaths and predisposes to avitaminoses, tuberculosis, pneumonia and many other diseases. Apart from its medical importance it is responsible for serious economic loss. Its prevention is being attempted.

Bilharzia is a chronic infective illness with many resemblances to syphilis and tuberculosis. It may attack practically every organ. Attention has been concentrated too much on the local symptoms in the bowel or bladder and the general constitutional symptoms have

been overlooked, so that diagnosis is often missed if local symptoms are absent or so mild that they are not observed by the patient. This applies especially to infestations with *Schistosoma mansoni*.

S. mansoni almost invariably involves the large bowel and is rare in the bladder. There may be no bowel symptoms, the patient stressing his lack of energy and loss of weight. Three main clinical varieties of these infestations exist in S. Rhodesia.

Group 1 is the largest, patients showing general symptoms, of which urticaria and pyrexia, occurring within a few weeks of exposure to infection, are the most important. The cercariae are then still in the blood. This invasive phase is called Katayama disease in Japan and elsewhere ; it continues for a few weeks and the diagnosis may be missed. The author describes what he believes to be the first instance of it to be reported from S. Rhodesia. The patient was a European boy, aged 10, who infected himself in a river. Three weeks later he had a sudden rigor (102°F.). The temperature rose each evening. Malaria, enteric and undulant fever were excluded. Four days after the rigor the penis began to swell and the next day there were urticarial swellings all over the body. The temperature continued, eosinophilia was 33 per cent. but no eggs could be found in the faeces or urine. After four weeks the temperature subsided and six weeks later eggs of *S. mansoni* were found in the stools. The combination of fever, urticaria and eosinophilia should call early bilharzia to mind. Later on general symptoms may occur, with eggs in the stools, but no bowel symptoms that the patient can observe. There may be early loss of weight (often severe in natives, who have the disease longer before it is diagnosed), early loss of appetite, flatulence and gastric pain (which may simulate peptic ulcer or chronic cholecystitis), debility and lack of energy, fever (an evening rise for one to several days), chronic cough due to irritation of the lungs by the eggs, which may result in fibrosis of the lung leading to dyspnoea and failure of the right heart [see this *Bulletin*, 1938, Vol. 35, p. 665]. Eosinophilia occurred in about one-third of Gelfand's cases, being less frequent in the later stages and only rarely high. Slight or moderate hypochromic anaemia may occur, and the blood sedimentation rate was increased in rather more than half his cases. Gelfand does not think mental retardation and epileptiform seizures are due to bilharzia.

In *Group* 2 the bowel symptoms are the chief complaints. Abdominal pain, periodic and usually mild diarrhoea with blood and mucus and eggs in the stools are found ; in a few Europeans and natives constipation may be the main trouble. The author does not think that haemorrhoids and pruritus ani are caused by *S. mansoni*.

Group 3 includes the late stages, which occur 10–30 years, or sometimes earlier, after infestation. Some of these patients have eggs in the liver which cause hepatitis, and, later, cirrhosis of the liver and splenomegaly (Egyptian splenomegaly), especially in natives. Cirrhosis may not develop for many years, being preceded by repeated attacks of transitory jaundice, which may closely resemble infective hepatitis ; at this earlier stage antimony may effect a cure, but it cannot do so when cirrhosis has developed. Death may then result from pneumonia, tuberculosis, cholaemia, portal thrombosis, cancer of the liver or haemorrhage. In other cases deficiency diseases or infective illnesses (pneumonia, tuberculosis) due to lowered resistance develop ; these have been found in natives only, because the European gets earlier treatment. *G. Lapage.*

SKRJABIN (K. I.) & MATHEVOSSIAN (E. M.). **Types of Topographical Correlations of Sexual Glands in Cestodes of the Family** *Hymenolepididae* **and their Taxonomic Significance.**—*C. R.* (*Doklady*) *Acad. Sci. URSS.* 1942. Vol. 36. No. 1. pp. 32–35. With 1 fig.

SKRJABIN (K. I.) & MATHEVOSSIAN (E. M.). **Stages in the Postembryonic Development of Cestodes of the Family** *Hymenolepididae* **and an Attempt to establish Morphological Types of their Larvicysts.**—*C. R.* (*Doklady*) *Acad. Sci. URSS.* 1942. Vol. 35. No. 3. pp. 83–85. With 3 figs.

SKRJABIN (K. I.) & MATHEVOSSIAN (E. M.). **Typical Morphological Modifications of the Chitinous Organs of the Scolex in Cestodes from the Family** *Hymenolepididae.*—*C. R.* (*Doklady*) *Acad. Sci. URSS.* 1942. Vol. 35. No. 3. pp. 86–88. With 1 fig.

VENZANT QUINTANA (Enrique). Infiltrado de Loeffler, provocado por el Necator Americano. [**Loeffler's Infiltration, caused by** *Necator americanus.*]—*Rev. Méd.-Quirúrg. de Oriente.* Santiago de Cuba. 1942. Sept. Vol. 3. No. 3. pp. 159–161. With 2 figs.

The author has already published, with CORDIÉS, accounts of three cases of transient pulmonary infiltration; he concluded that the infiltration was allergic. A further case is here described, the patient being a youth, aged 14, who complained of cough, pain in the shoulders and weariness. There was no fever and no other signs of disease were found. The patient's five brothers and both his parents were alive and well; he said that his family was free from tuberculosis. His lips were thick, his nose thick and eroded, his face doughy, as in the exudative diathesis. The lungs and heart were normal, but fluoroscopic examination showed a paracardiac infiltration of the base of the left lung, which was confirmed by radiography. Photographs illustrate this. There was an eosinophilia of 8 per cent. and the faeces contained eggs of *Necator americanus* and Trichuris. Anthelmintics with rest in bed and anti-anaemic treatment resulted after 13 days in the disappearance of the infiltration and of the eggs of Necator, but the eosinophilia was then 10 per cent.

The author thinks that the case showed the two characteristics of Loeffler's syndrome, namely, a transient infiltration and an eosinophilia which disappears with the infiltration. [This is not clear, because he states that the eosinophilia before treatment was 8 per cent., while it was 10 per cent. when the infiltration had disappeared.] In his earlier cases there had been little eosinophilia. He thought the case was allergic, the allergen being derived from the products of the parasites.

During the subsequent discussion FONSECA said that there could be a simple coincidence between eosinophilia due to parasites and transient infiltrations like those described earlier by Venzant. [See also this *Bulletin*, 1941, Vol. 38, pp. 538, 539.] *G. Lapage.*

HEILIG (Robert) & VISWESWAR. **Influence of Anti-Anaemic Treatment on the Gastric Function in Hookworm Disease.**—*Indian Med. Gaz.* 1942. July. Vol. 77. No. 7. pp. 385–390. With 6 figs.

It is believed, say the authors, that stomach function influences the condition of the blood, deficiency of HCl, for example, impairing the utilization of iron in the food; and that inability of the stomach

to form Castle's intrinsic factor, which is necessary for building the anti-anaemic or anaemia-preventing factor from the extrinsic factor, is one of the main mechanisms leading to pernicious anaemia. But, how, the authors ask, is the stomach influenced by changes in the condition of the blood? Practically nothing is known about correlation of haemopoietic and stomach functions in cases of hookworm anaemia undergoing iron treatment.

The authors studied this question in 51 hospital patients (43 men and 8 women) suffering from hookworm anaemia. On admission the number of erythrocytes, the haemoglobin values and gastric acidity were noted. Out of the 51 patients 37 were selected for further investigation, all of the selected ones being free from other active disease and afebrile, with a haemoglobin value on admission of not more than 20 per cent. (Sahli). The haemoglobin value, number of erythrocytes and gastric acidity of these 37 were noted every week during iron treatment (Blaud's pill, 90 grains a day) until the haemoglobin reached 30–40 per cent. This usually required 3–4 weeks. Anthelmintics (not specified) were then given. The results given below apply to patients before deworming.

Of the 37 patients studied further 7 (19 per cent.) were achlorhydric on admission, 10 (27 per cent.) were hypochlorhydric, 11 (30 per cent.) were normal and 9 (24 per cent.) were hyperchlorhydric. Graphs and tables show the condensed estimates of the haemoglobin, erythrocyte number and gastric acidity, the results being treated in three groups—achlorhydric, hypochlorhydric and a combination of normal and hyperchlorhydric.

In the achlorhydric group the averages of 7 cases showed, after 4 weeks of iron, increases of free HCl from 0 to 2; total acidity varied from 7 to 10; haemoglobin rose steeply from 14 to 39. In the hypochlorhydric group the averages of 10 cases showed, after 4 weeks of iron, a rise of free HCl from 5 to 6; total acidity remained constant at 15; and the haemoglobin rose from 16 to 40·6 per cent. In the normal-hyperchlorhydric group the averages of 20 cases showed, after 4 weeks of iron, that the free HCl remained practically unchanged (varying from 25 to 24), the total acidity varied from 36 to 33 and that the haemoglobin rose from 13·2 to 33·7 per cent. Comparison of the results with those of the earlier workers quoted and with values obtained from normal Indians indicates that among 51 cases of hookworm anaemia in Mysore the percentage having a gastric acidity below 20 free HCl is twice as high (42 per cent.) as it is among 91 normal Mysoreans (22 per cent.). The blood of 37 subjects of hookworm anaemia was greatly improved by 4 weeks of iron treatment, but the increase of free HCl was so small that it did not affect the efficiency of the stomach function. Similar facts are known regarding pernicious anaemia and idiopathic hypochromic anaemia, in which the changes in gastric function are, as in hookworm anaemia without deworming, irreversible. The improvement in the blood in these cases was independent of the gastric acidity; it occurred more quickly and extensively in the achlorhydric than in the normal-hyperchlorhydric group. Thus the average haemoglobin value on admission was lowest in the normal and hyperchlorhydric groups (13·2 per cent.) as against 16 per cent. in the hypochlorhydric and 14 per cent. in the achlorhydric groups. After 4 weeks of iron treatment, the haemoglobin value was lowest in the normal and hyperchlorhydric groups (33·7 per cent.) as against 40·6 per cent. in the hypochlorhydric and 39 per cent. in the

achlorhydric groups. Thus neither production of free HCl nor the *p*H of the gastric juice were deciding factors in the utilization of the iron. Actually the absolute increase in haemoglobin was highest in the achlorhydric group (25 per cent.). It was about the same in the hypochlorhydric (24·6 per cent.) and only 20·5 per cent. in the normal and the hyperchlorhydric groups. *G. Lapage.*

NIÑO (Flavio L.). Apendicitis verminosa por "Enterobius vermicularis." [**Verminous Appendicitis caused by** *Enterobius vermicularis.*] —*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1942. Sept. Vol. 18. No. 149. pp. 683–692. With 8 figs.

The author refers to his four earlier papers in which he emphasizes the importance of the part that may be played by parasites in the production of an appendicular syndrome. After reading the histories of the 24 cases of appendicitis ascribed to *Enterobius vermicularis* recorded in the Institute of Clinical Surgery at Buenos Aires, he is impressed by the fact that doctors may not diagnose the condition until they get the histopathological report, owing to lack of sufficient questioning of the patient and to excess of modesty of the patients, who may not mention the anal pruritus and its nocturnal exacerbations. It is not uncommon to find that removal of the appendix has not improved the condition of the patient. Systematic parasitological examination of all cases for which appendicectomy is proposed might detect the parasites and their treatment before or after the operation and would benefit the patients. In the subsequent discussion EGUES agreed with these views.

Niño describes two other cases which leave, he thinks, no doubt that *Enterobius vermicularis* can cause the appendicular syndrome.

The first case was an Argentine man, aged 32, who had had pain in the right iliac fossa for 15 years with nausea and vomiting. Periodical constipation, gastric dyspepsia and loss of red blood not mixed with the faeces and suggesting haemorrhoids were among the symptoms complained of. There was painful colic on deep palpation. Some sections of the excised appendix showed follicular hyperplasia of the submucosa. Others showed haemorrhagic foci with mucosal ulcers and submucous abscess. The microphotographs show sections of *E. vermicularis*. In one of them four worms are seen at the bottoms of two ulcers, which extend to the muscularis and there are portions of five other worms in the lumen. Other microphotographs show the head of a worm buried in a lymphoid follicle with tissue in its mouth. [The reproductions do not show this very well.]

The other case was an Argentine woman, aged 18, who had suffered for years from pains in the right iliac fossa extending to the right leg and hindering movement. She had had nausea and persistent constipation. There was pain at McBurney's point and a distended colon. One section of the excised appendix showed marked lymphoid hyperplasia without parasites or other apparent lesion. Another showed follicular hyperplasia with 13 worms in the lumen in intimate relation with the mucosa ; another showed a rather atrophied mucosa with seven worms in the lumen ; another showed three ulcers in the mucosa, one of which reached the muscularis and had a worm in its cavity and there were three worms in the lumen.

Of the 24 cases recorded at the author's Institute up to date, seven were males and 17 females, which corresponds with the greater frequency of *E. vermicularis* in females.

In the subsequent discussion JURADO said that 18 per cent. of a large number of cases of appendicitis collected by him were parasitic. REY described a case illustrating his view that amoebic infection may be a misleading complication of cases of appendicitis.

G. Lapage.

CHOMET (B.). **Oxyuris Vermicularis Infection of the Wall of a Fallopian Tube.**—*Arch. Pathology.* 1942. Oct. Vol. 34. No. 4. pp. 742–744. **With 1 fig.**

"A case is reported of infection of a fallopian tube by Oxyuris vermicularis, probably due to transport from the lower genital canal."

STOWENS (Daniel). **The Effect of Ultraviolet Irradiation on *Trichinella spiralis*.**—*Amer. Jl. Hyg.* 1942. Nov. Vol. 36. No. 3. pp. 264–268. **With 1 fig.** [10 refs.]

The author tried the effect of ultraviolet irradiation of the intestinal and muscle phases of *Trichinella spiralis*. HOLLAENDER, JONES and JACOBS have shown that it has an effect on *Enterobius vermicularis*.

Larvae of Trichinella were exposed in a quartz cup 12 inches away from a high frequency lamp giving rays between 2,650 and 3,200 Å, for periods varying between 5 and 120 minutes. These were given in food to mice, all the larvae being motile at the time. Controls were fed with larvae which had not been irradiated. Adults and larvae were then obtained from the infected mice. For the intestinal phases the mice were killed between the 3rd and 5th days after the irradiation of the larvae. The number of adults recoverable from the intestine was reduced from 14·8 per cent. less than the number found in the controls with an exposure of 5 minutes to 99·5 per cent. less with an exposure of 2 hours. The reduction in the number of adult worms recovered was commensurate with the length of the exposure to ultra-violet irradiation. There was no apparent morphological change in the adult worms which developed from irradiated larvae. For the recovery of larvae from the muscles of infected mice the animals were killed 4 weeks after infection and the larvae were recovered by McCoy's technique. The number of larvae in the muscles was reduced from 58 per cent. less than the number found in controls with an exposure of 5 minutes to 100 per cent. less [*i.e.* nil] with exposures of 1 and 2 hours.

Because the larvae were suspended in a gelatin-broth containing protein which absorbs ultra-violet rays, the procedure was checked by exposing larvae in distilled water on a glass slide to ultra-violet light. All the larvae thus exposed were killed in 10 minutes, although most of them survived an exposure of 6 minutes. The unexposed controls were alive after 10 minutes. Thus the gelatin broth protected the larvae considerably. The author suggests that the ultra-violet light may inhibit the enzymes of the larvae; it is known that it inhibits many enzymes of digestion and oxidation-reduction. Motility is not a criterion of infectivity because all the larvae given to the mice were motile at the time.

Thus, ultra-violet light impairs the ability of the larvae to establish themselves in the intestine and this is reflected in the reduction of the number of larvae found in the muscles. These effects increase with the increase in the time of exposure to ultra-violet light.

G. Lapage.

DEFICIENCY DISEASES.

Hou (H. C.). **The Dietary Intake and Urinary Output of Vitamin B_1 and their Relation to Beriberi among Chinese.**—*Chinese Med. Jl.* 1942. Jan.–Feb. Vol. 61. No. 1. pp. 6–18. [23 refs.]

Evidence is presented to support the now well-known fact that the amount of vitamin B_1 in a rice-eater's diet depends in the main on the degree of milling of the rice. [The losses in washing and cooking may, however, be comparable to those occurring during milling; see PLATT, "Rice and its importance in human nutrition," Appendix 6, first report on Nutrition in the Colonial Empire, Part I, 1939.] Records are given purporting to show that increase of beriberi in the early stages of the Sino-Japanese war occurred. [A survey in August, 1937, in refugee camps in Shanghai—Annual Report, 1937–1938 Henry Lister Institute of Medical Research, p. 20—revealed an incidence of 29 per cent. of refugees showing evidence of Vitamin B_1 deficiency; this incidence was similar to that in a sample of factory-worker population taken at the same time of the year in 1936.] The author remarks on a reduction in the death rate from beriberi in 1938 compared with 1937 and suggests that this may have been due to the introduction of treatment with pure Vitamin B_1. [Hou gives the case mortality rate from beriberi in Shanghai in 1936 as 39·11 per cent.; during this year the abstracter cured 17 cases of beriberi with crystalline Vitamin B_1—Platt, Annual Report, Henry Lister Institute of Medical Research, 1936, p. 24. These were all cases which had been notified to the Municipal Health authorities of the International Settlement of Shanghai and were of the type of beriberi which, up to that time, has always been considered to be fatal. The deaths recorded in 1936 increased by this number would have given a rate of 48·5 per cent. (*i.e.* about equal to that in 1937; so that it would have been more correct to say that a reduction in death rate had already been achieved in 1936 owing to the introduction of treatment with crystalline Vitamin B_1.] Various statements are made as to the level of excretion of Vitamin B_1 among Chinese on normal and on poor diets and for patients with various types of beriberi and other diseases. [The author gives no reference in the text to the method employed for this excretion data. Presumably from his earlier work he used the method developed by Yang and Platt, *Chinese Journal of Physiology*, 1939, Vol. 14, p. 259.] *B. S. Platt.*

Hou (H. C.). **Prevention and Treatment of Common Nutritional Deficiency Diseases.**—*Chinese Med. Jl.* 1942. Mar.–Apr. Vol. 61. No. 2. pp. 101–112. [12 refs.]

Some dietary deficiencies occurring in Shanghai are reviewed. The incidence is said to have increased during the war beginning in 1937. The nutrient content of various foodstuffs are tabulated. The author recommends a comparatively small dose of Vitamin B_1 for the treatment of beriberi. [The amounts of vitamin employed are similar to those worked out by the abstracter and fully described by him in the Annual Report of the Henry Lister Institute of Medical Research, 1936: see also *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1938, Vol. 31, p. 493, and the *Biochemical Journal*, 1939, Vol. 33, p. 1525.] *B. S. Platt.*

MEARS (A. R. R.). **Pellagra in Tsolo District.**—*South African Med. Jl.* 1942. Nov. 14. Vol. 16. No. 21. pp. 385–387.

The author describes a condition known to the Transkei natives as *keleba*, and identifies this with pellagra; he reports 59 cases. Three tribes are represented in the area and of these two are predominant and about equal in numbers, the Fingo and the Pondomisi, but nine-tenths of the cases of keleba were seen in the Pondomisi and over four-fifths were in women. The reason for this distribution is not clear; the diets are similar except that the Pondomisi, who do not affect European dress, drink much more Kaffir beer (three-quarters of the patients admitted heavy drinking) than the Christianised Fingo. The seasonal incidence is marked in the last quarter of the year; the main beer season is after the harvest in July and August.

Symptoms were stomatitis, enteritis and rash. The stomatitis was typical, with redness and painful ulceration of the lower lip, sore tongue and throat, and excessive salivation. The rash presented the usual appearance of harsh desquamating plaques on exposed surfaces; in two women there was a genital rash. Enteritis was diagnosed on abdominal pain, usually with diarrhoea. Insanity was not common, but the general condition may be very bad in acute cases. In chronic cases there is the impression of general ill-health and the objective signs may be slight or absent.

Dietetic treatment was impossible, but the author found that nicotinic acid produced dramatic results, especially in acute cases. The dosage was 100 mgm. daily but the optimum is probably 150–200 mgm. daily. He notes that in certain cases with œdema of the face and extremities the response was slow, and suspects, in these cases, other deficiencies such as of vitamin B_1. *C. W.*

HAEMATOLOGY.

TROWELL (H. C.). **Deficiency Anaemias of Malnutrition.**—*Lancet.* 1943. Jan. 9. pp. 43–46. With 1 fig. [31 refs.]

The common malnutrition anaemia of the tropics is a macrocytic orthochromic anaemia, which, when complicated by an iron-deficiency (which it often is), gives a confused picture for which the term, dimorphic anaemia is suggested by the author. Nutritional macrocytic anaemia is due to a deficiency of extrinsic factor in the diet and though more common in pregnancy and in the tropics it may be seen in both sexes at all ages, in all climates and among all races. It may be missed if the colour index is about or below unity and if the mean red cell diameter is normal. In these cases an estimation of the mean corpuscular volume, which is always increased, will establish the diagnosis. Mild cases should improve with an improvement in the diet if it is recognised that meat is the only rich source of extrinsic factor. Severe cases must be treated with some form of liver or a yeast preparation. They are refractory to many forms of liver in the form and dosage active in pernicious anaemia, and this may cause confusion in diagnosis with achrestic anaemia, acquired acholuric jaundice and aplastic

anaemia. The author has found intramuscular liver extract (B.D.H.) 5–10 cc. weekly, or " Campolon " 8–15 cc. weekly, successful in non-pregnant cases; where there is severe haemolysis or pregnancy a larger dosage (*e.g.*, 42–56 cc. of " Campolon ") is required. The author found " Anahaemin " successful in non-pregnant cases in a dosage of 12 cc. weekly; there was a moderate response to 6–8 cc. and no response to 4 cc. Marmite is effective, but since 30–60 gm. daily is required, it has been largely replaced by liver injections. For the African patients liver by mouth (½ lb. daily) is the method of choice, since it is much cheaper and supplies other dietary deficiencies. In European patients liver injections are better since they are more certain and swifter in action.

H. N. Green.

PIERAERTS (G.). Etude sur le syndrome depigmentation-oedème au Kasai. [**The Syndrome of Depigmentation and Oedema in Kasai.**] —*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 104–112. Discussion pp. 112–124. [52 refs.]

The author believes that the syndrome, with its depigmentation, anaemia, oedema and digestive disturbances, is produced by shortage of iron, and may be due primarily to a deficiency of the element in the diet, or secondarily to mal-absorption consequent upon gastro-intestinal disturbances, or to a negative balance associated with chronic haemorrhage. He postulates that the pigment of the skin is derived from chromagens through the action of enzymes for which iron, or a copper-iron couple, is a necessary co-enzyme. Deficiency of iron disturbs not only erythropoiesis and leucopoiesis but also other enzyme activities of the organism and particularly those of the skin, and is related therefore to dryness and wrinkling of the skin, loss of pigmentation, exfoliation of the nails and loss of hair. In the negro it is more obvious than in the European because the former requires more of the co-enzyme by reason of his greater pigmentation. There is no evidence that hookworms exert a toxic effect on haemopoietic function. The disturbances they produce are due to the losses they cause and particularly losses of iron. [See this *Bulletin*, 1942, Vol. 39, p. 99.]

F. Murgatroyd.

HEILIG (Robert) & VISWESWAR (A.). **Iron-Refractory Anaemia in Hookworm Disease.**—Reprinted from *Indian Physician.* 1942. Aug. Vol. 1. No. 8. p. 359 in *Jl. Trop. Med. & Hyg.* 1942. Aug. 1. Vol. 45. No. 15. pp. 113–116.

In Mysore, patients harbouring hookworms commonly show a hypochromic microcytic anaemia which rapidly and regularly responds to iron, a 10 per cent. (Sahli) rise in haemoglobin being produced within a fortnight by 90 grains of Blaud's pill daily, provided neither vomiting nor diarrhoea interferes with the absorption of the drug. Patients failing to respond [*i.e.* those with iron-refractory anaemia] are found almost invariably to be suffering from additional infections, of which the commonest are malaria and infections of the urinary tract, ear or sinuses. Such infections must be treated if the anaemia is to respond adequately. The presence of the hookworms does not prevent the response to iron although in order to maintain the improvement in the anaemia the worms must be removed. The importance of dealing first

with the anaemia lies in the observation that toxic effects of carbon tetrachloride or tetrachlorethylene have only been encountered in patients whose haemoglobin levels were below 40 per cent.

F. Murgatroyd.

MORRISON (Maurice), SAMWICK (A. A.) & LANDSBERG (Eva). **Sickle Cell Anemia in the White Race. Report of Two Cases with Diagnosis by Splenic Puncture.**—*Amer. Jl. Dis. Children.* 1942. Nov. Vol. 64. No. 5. pp. 881–887. With 4 figs.

Two cases of sickle cell anaemia occurring in two American families of Italian descent are described, thus adding to the 13 previously reported examples of the condition in white persons in whom it is claimed that an admixture of negroid blood could be excluded.

The first patient was seen at intervals over a period of 7 years, during which time she suffered from various attacks of abdominal colic, joint pains, pneumonia, frequency of micturition with haematuria and pyuria. The blood showed an anaemia and a leucocytosis. The underlying condition was for some time overlooked as the patient was white, and sickling was not observed during earlier direct examinations of the blood. For similar reasons the second patient's condition was at first mis-diagnosed. She was originally thought to be suffering from a haemolytic anaemia due to sulphanilamide which had been given in the treatment of an attack of tonsillitis. Recurrence of the haemolytic anaemia 10 months later in the absence of any drug suggested the possibility of the condition being one of haemolytic jaundice. The red cell fragility was not increased and the exact diagnosis remained in doubt until sickle cells were observed in preparations from a splenic puncture. It is suggested that sickle cell anaemia should be considered in all obscure haemolytic disorders even in white persons.

F. Murgatroyd.

WEINGARTEN (R. J.). **Tropical Eosinophilia.**—*Lancet.* 1943. Jan. 23. pp. 103–105.

Since 1934 the author has seen in India 81 patients suffering from what he believes to be a new disease. The illness starts with lassitude, anorexia, evening fever and loss of weight. After some days a paroxysmal dry cough, expiratory dyspnoea which may last weeks, and sometimes recurring attacks of nocturnal asthma develop, the physical signs resembling those of asthma. The sputum is scanty, tenacious and muco-purulent with no organisms of any significance ; it frequently contains clumps of eosinophil cells but Charcot-Leyden crystals and Curschmann spirals are rarely seen. X-ray examination from the 4th to the 6th week shows disseminate mottling of both lung fields, especially marked at the hilar regions and at the bases ; an average single focus is about the size of a split pea and has a moderately intense central shadow and an ill-defined and blurred outline. The blood shows a most marked eosinophilia, which is responsible for the considerable leucocytosis ; the percentage of eosinophil cells, in one case as much as 88 per cent., is higher than in any other disease except eosinophilic leukaemia. No parasites are to be found in the blood, and the stools and urine show nothing unusual. There may be a mild secondary anaemia, the erythrocyte sedimentation rate is moderately increased, the blood chemistry is normal and the spleen is slightly enlarged.

The disease, not infrequently diagnosed as chronic phthisis or bronchial asthma, runs a benign course, although if untreated it may last for years. It is not considered to be an allergic manifestation and has no connexion with Loeffler's syndrome [see this *Bulletin*, 1942, Vol. 39, p. 792.] The cause has not yet been determined.

Treatment was symptomatic until the administration of neo-arsphenamine to a patient suffering also from syphilis was followed by subsidence of the respiratory symptoms and a fall in the leucocytes from 64,200 to 7,800 per cmm., representing a decrease in the eosinophils from 71 to 16 per cent. Arsenical treatment of other patients suffering from the syndrome was then undertaken and the results were similarly favourable. There appear to have been no relapses.

The aetiology is unknown, but most of the patients seen lived near the sea. *F. Murgatroyd.*

VENOMS AND ANTIVENENES.

VELLARD (J.). Modificaciones sanguineas provocadas por los venenos. Acción hemolitica y variaciones de la resistencia globular *in vivo*. [**Blood Changes set up by Snake Venoms. Haemolytic Action and Changes in Corpuscle Resistance (to Haemolysis).**]—*Rev. Inst. Bacteriológ. "Dr. Carlos G. Malbran."* Buenos Aires. 1942. Dec. Vol. 11. No. 2. pp. 144–167.

[The information given in this article is already very condensed and hence is difficult to abstract. The results of a large number of very interesting experiments are presented in protocols and should be carefully studied by all working on the effects of snake poisons on the blood. To convey an adequate idea of the experiments would necessitate reproduction of many of these protocols and we must consequently limit ourselves to the main outlines of the investigation.]

Twelve samples of venom have been studied : *Naja tripudians* from Bombay ; *Elaps lemniscatus* (Coral snake) from N.E. Brazil ; *Lachesis muta* from N.E. Brazil ; *Crotalus terrificus* from Venezuela, N.E. Brazil, Central Brazil, and the Argentine, four samples ; *Bothrops atrox*, Venezuela and N.E. Brazil, two samples ; *B. jararaca* from Rio de Janeiro ; *B. erythromelas* from N.E. Brazil and *B. alternata* from the Argentine. The investigation included : (1) The haemolytic power of serum of dogs (which were the animals used for these experiments) on normal corpuscles collected and washed before addition of the venom. (2) Haemolytic power of the serum on washed sheep-cells. (3) The same for the horse. (4) As (1), but with added venom. (5) Corpuscle resistance to hypotonic solutions. (6) Corpuscle resistance to the haemolytic action of the venom in the presence of normal horse-serum.

The venoms are grouped as regards haemolysis and coagulation into three categories :—

1. Haemolytic but not coagulant : *N. tripudians, E. lemniscatus.*
2. Haemolytic and coagulant : *C. terrificus, L. muta, B. atrox* and *B. erythromelas.*
3. Coagulant and non-haemolytic (or very slightly so) : *B. alternata, B. jararaca.*

Not only do the poisons of different species vary in action, but specimens of the same species from different localities also vary. Thus, *C. terrificus* poison in a Pernambuco specimen has little or no proteolytic action, and its coagulant and haemolytic actions are less than those of Venezuelan specimens; poison from an Argentine *C. terrificus* is markedly coagulant *in vitro*, but less haemolytic than that from Pernambuco, and that from a Central Brazilian specimen was very feebly haemolytic and had no proteolytic action.

To sum up: Venoms with marked phosphatidase properties but non-coagulant, as *N. tripudians*, produce in the dog strong haemolysis—"positive phase"—which is always brief; then follows a "negative phase" in which phosphatids are destroyed and the haemolytic properties disappear and the corpuscle resistance returns to normal. The lowered resistance of the positive phase is due to circulatory haemolysins and the poison acts directly on the corpuscle phosphatids, just as it does on those of the plasma. The red cells increase in volume without spontaneous haemolysis, but the resistance to the venom haemolysins is reduced; then the second, negative, phase sets in and the corpuscle resistance progressively increases. The rapidity of the change depends naturally on the mode of introduction of the venom and the dose, but it may be said that autohaemolysins rarely persist in the circulation for more than an hour (average 30–45 minutes), but regeneration of the phosphatids is always gradual, taking more than 24 hours. [See also this *Bulletin*, 1942, Vol. 39, p. 885.]

H. Harold Scott.

TRETHEWIE (E. R.). **Tissue Injury by Trypsin.**—*Australian Jl. Experim. Biol. & Med. Sci.* 1942. Mar. Vol. 20. Pt. 1. pp. 49–54. With 5 figs. [19 refs.]

This is a very interesting but highly technical article, and those wishing to confirm the author's results should consult the original for details of the experimental work.

Agents which cause tissue injury, snake venom, for example, liberate several pharmacologically active substances, histamine, lysocithin, adenyl compounds, an inactivating enzyme and others. The author has carried out investigations to see if the liberation of certain of these substances could be ascribed to specific attributes of the injurious agent. He has previously shown that the property of snake venom of liberating histamine and what he designates "slow reacting substance" (S.R.S.) is paralleled by its haemolytic activity. Trypsin injected into the excised liver of a rabbit by an intraportal cannula liberates S.R.S., adenyl compounds and an inactivating enzyme. Trypsin is proteolytic in action and alters the permeability of the cell-membrane and inner cell structure, thus liberating the substances mentioned. In other words, trypsin is a proteoclastic enzyme which acts on the lipoprotein of the cell membrane and cell substance.

The application of these findings to the action of snake venom is that in the venom, as FELDBERG and KELLAWAY have demonstrated, is a lipoclastic enzyme which will split off oleic acid from lecithin to form lysocithin, lecithin itself being a constituent of cell membrane, and lysocithin has a powerful haemolytic action. "In view of the similarity of the substances liberated by trypsin and by snake venom

it is perhaps not surprising that few conditions produce so rapid and so severe a state of 'shock' as severe snake bite." [See also this *Bulletin*, 1939, Vol. 36, pp. 564, 565.] *H. Harold Scott.*

DERMATOLOGY AND FUNGOUS DISEASES.

VOLK (Ricardo) & CANAS (Eugenio). Un caso de blastomicosis. [**A Case of Blastomycosis.**]—*Medicina.* Mexico. 1942. Dec. 25. Vol. 22. No. 426. pp. 615–623. With 7 figs.

The case here recorded as blastomycosis should perhaps be classed as Geotrichosis in view of the fungus isolated and grown from the lesions—a species (unnamed) of Geotrichum. The patient was a man of 33 years who, at the age of 20, received a blow on his left foot which, he said, "splintered the bone," but was healed by moist applications and ointments. The place broke out and healed again from time to time during eight years, and he then went to hospital where the "bones were scraped" and healing again followed. After that small swellings appeared on the dorsum of the foot and discharged pus, then cicatrized and broken down on and off for 5–6 years and he underwent the "scraping operation" again. Four years ago three swellings appeared on the left thigh, about 5 cm. in diameter, which suppurated and discharged a gummy material. A variety of treatments were tried—rubiazol, solusalvarsan, bismuth injections, potassium iodide in large doses internally, but all were ineffectual. They are now papules or pustules, 8 cm. in diameter, and increasing slowly 1–2 cm. a month; they appear as agglomerated minute abscesses with yellow points, at times dark red to violet. There are also papillomata over the metatarso-phalangeal articulations of the left foot, and in the groin enlarged glands, not adherent. The patient states that the lesions are painless and he has had no fever. Several reactions for syphilis—Wassermann, Kahn, Kline, Meinicke and others—have been tested with uniformly negative results. A species, not identified, of Geotrichum was grown on Sabouraud's medium with 2 per cent. glucose. *H. Harold Scott.*

CARRIÓN (A. L.). **Chromoblastomycosis.**—*Mycologia.* 1942. Vol. 34. No. 4. pp. 424–441. With 6 figs. & 1 diagram. [Summary taken from *Rev. Applied Mycology.* 1943. Jan. Vol. 22. Pt. 1. p. 23.]

After reviewing the history, geographical distribution, and clinical features of chromoblastomycosis, the author states that repeated observations on many isolates from different parts of the world show that sporulation in the fungi associated with the disease may be of the *Hormodendrum* (*Cladosporium*), *Phialophora*, or *Acrotheca* type. A few of the fungi concerned appear to sporulate by one or other of these methods exclusively, but in most of them at least two occur simultaneously in the individual isolates. The organisms behaving in this manner have been classified as two species of *Fonsecaea*, *F. pedrosoi* (Brumpt) Negroni and *F. compactum* Carrión (represented by one isolate).

The different types of sporulation characteristic of *F. pedrosoi* do not occur in the same proportion in all strains, and the group has therefore been subdivided into a number of varieties in accordance with the predominant method of sporulation.

F. pedrosi var. *typicus* corresponds morphologically with Brumpt's original description of *H. pedrosoi*. In this fungus, the *Acrotheca*-like sporulation reaches its highest development, the *Hormodendrum* heads are scant, abnormal, or depauperate and the *Phialophora* stage rare or missing. In *F. pedrosoi* var. *cladosporioides*, *Hormodendrum* is the predominant character. In *F. pedrosoi* var. *phialophorica* (originally described as *P. macrospora*) the *Phialophora* method of sporulation predominates, while typical *Acrotheca* heads are produced and *Hormodendrum* is wanting. Lastly, *F. pedrosoi* var. *communis* shows all three methods of sporulation, and includes numerous integrating forms which represent connecting links among the other three varieties.

As regards the proper generic name for these fungi, differences of opinion exist as to whether it should be *Hormodendrum*, *Phialophora*, or *Fonsecaea*. The objections to the use of *Hormodendrum* are that it would not admit certain isolates of the varieties *typicus* and *phialophorica*, in which the *Hormodendrum* sporulation has become obsolete, and that its application to the species *pedrosoi* has been responsible for most of the confusion. Inclusion in *Phialophora* would be even more confusing. Among the numerous specimens of *pedrosoi* so far studied, only in one does the *Phialophora* sporulation predominate. The author suggests that, as a matter of convenience, *Fonsecaea* is the most suitable name. The genus is legitimate and comprehensive, and covers without strain all varieties of the species *pedrosoi*. It represents a mycologic group possessing distinct pathogenic properties.

The *phialophorica* variety is accordingly named *F. pedrosoi* var. *phialophorica*, with a Latin diagnosis, synonyms being *P. macrospora*, *P. verrucosa*, and *Acrotheca pedrosoi*.

CALDWELL (G. T.). **Secondary (Granulomatous) Coccidioidomycosis—Coccidioidal Granuloma.**—*Texas State Jl. Med.* 1942. Oct. Vol. 38. p. 376. [Summary taken from *Jl. Amer. Med. Assoc.* 1942. Dec. 26. Vol. 120. No. 17. p. 1434.]

Caldwell discusses the 7 cases of coccidioidal granuloma that he has had occasion to study. Three of them were reported in 1932, and the other 4 are reported for the first time. He states that certainly 5 of the 7 patients contracted the disease in Texas. The histories of the other 2 are inadequate to conclude where the infection occurred: in 1 it is probable that the infection was acquired in California, while in the other 1 there are no data concerning place of residence or travel, and none can be secured. In none of the 7 is there any definite evidence that the primary infection occurred in the skin, although in one instance ulcers of the legs, which were thought to be varicose ulcers, might possibly have served as the port through which the chlamydospores of Coccidioides immitis entered. However, this seems unlikely. Most of the 7 patients had an initial acute coccidioidomycosis which involved the respiratory passages. If the ratio of acute cases of coccidioidal granuloma is around 300 to 1 or even 700 to 1, an appalling number of them are being overlooked in the various communities from which coccidioidal granuloma is reported.

MISCELLANEOUS.

FORD (Edward). **Medical Conditions on Bathurst and Melville Islands.** *Med. Jl. Australia.* 1942. Sept. 12. 29th Year. Vol. 2. No. 11. pp. 235–238. [10 refs.]

These large islands lie directly to the north of Darwin, Australia, and are separated from the mainland by 50 and 17 miles respectively, yet, since no permanent white settlement has persisted there, the tribal system has not been broken down. There have been contacts with Asiatic peoples, probably for centuries, and in recent years the crews of Japanese pearling vessels have visited the islands and have left Japanese-aborigine children, the oldest of whom was about 9 years of age when seen in 1939.

For the most part the health and physical condition of the natives are good ; adults are sturdy and well nourished, infants are robust. There is a period, however, between the ages of 2 and 5, when mortality is relatively high, and when injudicious feeding, in the period of transmission between weaning and the proper assimilation of the unmodified adult diet which is given after weaning, appears to cause ill health aggravated by the effects of hookworm infection which is particularly evident at this period. Hookworm is widespread in both islands, the eggs being found in 108 of 114 specimens, and an average haemoglobin value of 53 per cent. was found in 33 children examined. Respiratory diseases are common, and tuberculosis, both of the lungs and of the cervical glands, was seen ; there were a few cases of leprosy.

The situation with regard to malaria is peculiar. The author found no evidence of it, in the form either of enlargement of the spleen, or of positive blood smears, yet there are records of epidemics of subtertian malaria in the 19th century and in 1911. No mention of anophelines is made. Yaws is fairly common. Suppurative conditions are prevalent, especially in the wet season ; the destructive skin disease of the face [known as *bila bila*] was seen [for a description see this *Bulletin*, 1941, Vol. 38, p. 536].

Venereal diseases include ulcerating granuloma of the pudenda, and many patients suffering from this have been taken to Darwin for treatment. Gonorrhoea is found, but no evidence of syphilis was seen. *C. W.*

EBOUÉ (Félix). Discours en conseil d'administration, Afrique Equatoriale Française (Afrique Française Libre), 19 Novembre 1942. [**Health Services of French Equatorial Africa.**]—36 pp. [Service de Santé p. 16.]

In this speech the Governor-General makes references to the health services of French Equatorial Africa and to the difficulties they are compelled to face. The reduction in medical staff caused by the transfer of 30 medical men to the Fighting French forces or elsewhere, has necessitated the closure of 18 medical posts. Difficulties of re-equipment of the existing services are becoming greater, and war obligations, such as the cultivation of cotton and the production of rubber, have interfered with the prophylaxis of trypanosomiasis because of the concentrations of population they have entailed. Nevertheless, the organization remains active and effective. *C. W.*

CARPENTER (Stanley J.). **Mosquito Studies in Military Establishments in the Seventh Corps Area during 1941.**—*Jl. Econom. Entom.* 1942. Aug. Vol. 35. No. 4. pp. 558–561. With 1 fig.

SINTON (J. A.) & SHUTE (P. G.). **Memorandum on Measures for the Control of Mosquito Nuisances in Great Britain.**—Ministry of Health. Memo. 238/Med. Revised Oct., 1942. 32 pp. With 2 plates & 2 maps. 1943. London: H.M.S.O. [6*d.*]

This memorandum was first published in 1940 and, supplies being exhausted, it has been reprinted with some additional information. It is useful both to the entomologist as a summary of practical information and to the medical officer or sanitary inspector as a guide to the mosquitoes liable to become serious pests. The publication of such a booklet in war time is also valuable because troops returning to this country from malarious regions might possibly cause an outbreak similar to that associated with the last war. Two maps given in this edition show that the areas of England and Wales in which the cases then occurred correspond very closely with the areas affected during the 18th century. The explanation appears to be that indigenous malaria in England is restricted to localities infested with *A. maculipennis.*

For each of the biting species of British mosquitoes, the habits, distribution and specific measures of control are given (in more or less detail according to prevalence). There is also a useful chart showing at a glance what stages of these species are to be found in different months of the year.

The general section on Control gives extensive instructions for dealing with adults and with larvae, and this edition also includes measures against larvae in static water tanks and bomb craters.

Three useful appendices recount (i) the differences between anopheline and culicine mosquitoes, (ii) the methods of collection and transportation for identification of specimens, and (iii) some information on other bloodsucking flies. *J. R. Busvine.*

ROY (D. N.) & GHOSH (S. M.). **Further Work on the Comparative Efficacy of Different Culicifuges under Laboratory Conditions.**——*Parasitology.* 1942. Nov. Vol. 34. Nos. 3/4. pp. 291–294.

Continuing their studies on repellents for mosquitoes [ROY, GHOSH and CHOPRA, this *Bulletin*, 1942, Vol. 39, p. 795] the authors have made comparative tests in the laboratory on a long series of formulae proposed by various authors, together with a series of essential oils and other substances. The results are set out in tabular form. As in the earlier work, mixtures containing pyrethrum were effective for much longer than anything else tested. For example, MacNay's preparation (concentrated extract of pyrethrum, ½ oz.; castor oil, 4 oz.; citronella oil, 5 drops) remained active for five hours. Of the essential oils, clove oil was the best. The deterioration of pyrethrum on exposure to light is mentioned as a disadvantage. In stock mixtures it is stable provided the medium is neutral.

V. B. Wigglesworth.

WANSON (M.). Sur la biologie des phlébotomes congolais. [**On the Biology of Species of *Phlebotomus* in the Congo.**]—*Rec. Travaux Sci. Méd. Congo Belge.* Léopoldville. 1942. Jan. No. 1. pp. 23–43. With 6 figs. & 5 photos on 2 plates. [66 refs.]

The author's notes on the biology of the larvae and adults of several species of Phlebotomus are based on observations made in the field and on laboratory experiments. It seems probable that the work was done at Matadi, Belgian Congo.

In general, the author regards it as well established that the larvae of most species of Phlebotomus feed on ordinary vegetable material, and that they have no need of nitrogenous waste of animal origin. He has given a considerable amount of attention to *P. schwetzi* and has reared it on living moss and actually observed green material in the gut of the larva. But he has reared the same species and others on dead leaves, including the rather hard leaves of the mango; dead leaves are gnawed in a characteristic way. He has also reared the same species in garden earth [no facts are given about the organic content]: another favourable material is the very fine deposit from septic tanks in which active decomposition has ceased. On this he has reared several species, including *P. schwetzi* and *squamipleuris* for several successive generations: it is stated that this material is very rich in decomposed cellulose and that the nitrogen value is very low, but no analyses are given. On the other hand he has failed to rear *P. schwetzi* on a mixture of earth and blood, on lizard droppings, green leaves, powdered insects and cow dung either fresh or partly dry.

In nature early stages have been found in small numbers in the soil in cavities in rocks: dead leaves showing unmistakable signs of having been gnawed were sometimes but not always present. Larvae have not been found in nature in green moss.

Adults in captivity pair either before or after the female has taken a blood meal. Eggs are laid 30–36 hours after the meal. They are laid on the surface of the breeding material, in contact with one another but not in a heap, and the total number is 30–40. The egg stage lasts 6–8 days and the larval 35–40 days at about 28°C. The full-grown larva looks for some dry environment in which to become a pupa, pupal life lasting 8–14 days. Males and females are produced in about equal numbers, neither sex tending to emerge before the other. At Matadi and Thysville, *P. africanus* was the species most commonly captured; *schwetzi*, *squamipleuris* and *wansoni* were not infrequent, and four other species appeared to be rare. The species differed from one another in their habits in many respects. For instance, some are attracted by light; others (*e.g.*, *P. schwetzi*) are not. Some species do not enter houses, and two are apparently cave dwellers, feeding on bats, as is shown by the precipitin reaction. It is well known that *P. schwetzi* feeds on man, often biting in the afternoon, but it seems that the same species feeds readily on the dog and on laboratory mice, but not on hens, guineapigs or rabbits: there is also evidence from precipitins that this species will feed on bats and lizards. *P. africanus* also occasionally bites man [which is surprising, for the members of the group to which it appertains feed for the most part on reptiles]. The author finds that sandflies will hardly ever feed in a cage of a cubic foot or so. They will readily feed if they are confined in a small glass tube with a lizard, or if the tail of a mouse is introduced through a hole in the cork.

The author has produced a considerable increase in our knowledge of these insects. *P. A. Buxton.*

CANNON (D. A.). **Linguatulid Infestation of Man.**—*Ann. Trop. Med. & Parasit.* 1942. Dec. 31. Vol. 36. No. 4. pp. 160–167. With 3 figs. on 2 plates. [36 refs.]

The author reports on the colon of an African woman from Southern Nigeria. It was greatly enlarged and thick-walled, and studded with very great numbers of cysts of the Linguatulid, *Armillifer* (*Porocephalus*) *armillatus*. These were also present in great numbers throughout the thickness of the wall of the colon and in the mucosa. They had also been observed at post mortem, though in lesser numbers, at many sites under the visceral and parietal peritoneum. The patient had originally come into hospital complaining of alternating diarrhoea and constipation, evidently caused by subacute obstruction due to this great load of parasites.

The very remarkable appearance of the specimen is shown in several photographs. The paper includes a full review of the occurrence of Linguatulidae in man. *P. A. Buxton.*

BOOK REVIEWS.

MANSON-BAHR (Philip) [C.M.G., D.S.O., M.D., F.R.C.P. (Lond.), Senior Physician to the Hospital for Tropical Diseases, Royal Albert Dock & Tilbury Hospitals, etc.]. **Synopsis of Tropical Medicine.**—pp. xii+224. With 5 plates. 1943. London, Toronto, Bombay, Melbourne & Sydney: Cassell & Company, Ltd., 210, High Holborn, W.C.1. [7*s*. 6*d*.]

Every medical man intending to practise his profession in the tropics takes with him one of the larger text-books on tropical medicine and the majority decide on *Manson's Tropical Diseases*, the most comprehensive work in a single volume, hoping that someone else or the local medical library will have STITT's two-volume work. The editor of the former, Sir Philip MANSON-BAHR, has now written a *Synopsis of Tropical Medicine* which no medical man proceeding to the tropics can afford to leave behind. It is a veritable *plurimum in parvo*, yet it will not materially add to his luggage, because it can be slipped into the pocket. In fact it is best carried there, for it is a *vade mecum* which must not be inadvertently overlooked when he goes on trek or has to travel light and leave the larger books behind. For purposes of pre-examinational revision it is ideal.

It is difficult to avoid hyperbole in reviewing this work. Many synopses are so condensed that they become of little more interest than the dull reading of a catalogue—lists of causes, symptoms, diagnostic features and treatment. The book under review never falls to this level. The facts have been carefully marshalled and have been put together in a form eminently readable. The arrangement is orderly and sequential and the subjects dealt with so grouped as to

leave out no disease of importance. Protozoal, spirochaetal, rickettsial and bacterial diseases are considered in turn; then virus diseases, fungal infections, nutritional and climatic diseases in this order, and a short miscellaneous group of, at present, undiscovered causation. Vegetable and animal poisons are described interestingly and fully enough for general purposes; the final chapters, except for a short concluding one on Laboratory Methods, are concerned with metazoal infections, chiefly helminthic. There are five plates, well chosen for the importance of the subjects depicted, namely the different malaria plasmodia, intermediary hosts—mosquitoes, flies, ticks, snails—human intestinal protozoa, and the fifth of twenty-two helminth ova, drawn to scale.

There are a number of verbal slips, as is almost inevitable in these days when few people can devote much time to proof-reading, but these do not detract from the medical value of the work, for the facts themselves are all there and the verbal corrections can easily be made when the next edition is published. Little of importance has been omitted. Doctors going to the middle East might hope to find mention of Bejel, puzzling cases of which may come their way; no reference is made to the bone lesions of chronic melioidosis. Fontana's stain is mentioned more than once in the text as a means of diagnosis; this might with advantage be given in the short section on Methods.

Just 2,000 years ago Horace wrote: *Brevis esse laboro, obscurus fio* and there is always a risk of obscurity in striving after terseness. Generally speaking, this *Synopsis* is clear and definite in its statements, but occasionally we have been puzzled as to the meaning of a phrase or doubtful of its exact interpretation. For example: "*L. tropica* in numbers in macrophages of leucocytes beet" (p. 21): again, "Incubation period short: 2–8 days; after sexual contact prolonged to 12 weeks" (p. 95), where the absence of a comma makes a lot of difference. "Cuticle with spines anterior (oral): median muscular ventral sucker, former larger" (p. 161).

"T.B." stands, of course, for the tubercle bacillus; it is a pity to use the letters for the disease it sets up and may lead to confusion, as in "Differentiation of Blastomycosis from T.B." The mosquito *A. maculipennis* is said to be *androphilic* (p. 11). This is an understatement, for it is equally gynaecophilic. It is better to use the word "anthropophilic" which covers both. Kupffer (pp. 5, 15, 166) has no modification; solar (p. 137) should be "solah": the hooklets of *Taenia solium* are described as "rose thorn" (p. 198), whereas these are characteristic of Dipylidium. It is good to see "scoleces" spelt correctly.

The above are all comparatively small matters and do not seriously detract from the excellence of the work. The statements are dogmatic and rightly so when made by so eminent a specialist as the author. Attention may be drawn to specially useful points, such as common mistakes in the diagnosis of liver abscess (p. 39), the classification of the typhus fevers (pp. 56, 57), the schematic summary of the life-history of Strongyloides (p. 180), the rarity of Diphyllobothrium anaemia, of which the text-books usually make so much.

The format of the book leaves nothing to be desired: it is handy in size, the print, even the smallest, is very clear and the Index full and complete. In conclusion, the author has earned our thanks and is to be heartily congratulated on a difficult task well conceived and admirably executed. *H. Harold Scott.*

BRAHMACHARI (Upendranath) [Kt., M.A., M.D., Ph.D., F.R.A.S.B., F.N.I., Professor of Tropical Medicine, Carmichael Medical College, etc.]. **Gleanings from My Researches. Vol. I. Kala-Azar, its Chemotherapy.**—pp. xx+461. With numerous plates, charts & diagrams. 1940. Published by the University of Calcutta. [30*s*.]

In two volumes the author has gathered together a number of his published papers on the subject of kala azar and malaria and promises a third volume to include his papers on other subjects. His reason for reprinting the papers in book form is his desire "to infuse the spirit of research into the minds of students of medicine in India and not least among those whose paths are restricted to institutions where proper facilities for research are not available."

The first volume contains a series of the author's papers on kala azar particularly with reference to the chemotherapy of the disease and the studies which culminated in the discovery of ureastibamine and the demonstration that it was, at the time, the best remedy for the treatment of this condition. There is no doubt that this drug, though replaced by others which in the opinion of some observers are more certain and effective remedies, has been responsible in India for the saving of thousands of lives. One of the papers is that which describes a new form of cutaneous leishmaniasis to which the author gave the name dermal leishmanoid. This condition had escaped notice but is now known to be quite common in India as a sequela of kala azar, especially in treated cases which have been apparently cured of the visceral infection. Presumably leishmania have not been eradicated from the skin where, in a year or two after the supposed cure of kala azar, they produce a variety of cutaneous lesions. Another subject is that dealing with the precipitation of globulin from the serum of patients with kala azar when this is diluted with distilled water. From these observations the author elaborated his globulin opacity test for kala azar.

The papers reproduced in this volume have been reviewed from time to time in this *Bulletin*, but their collection in one place will be of great convenience to those who are interested in the historical development of our knowledge of kala azar in India, where the author has carried out all his investigations. *C. M. Wenyon.*

WILSON (Charles Morrow). **Ambassadors in White. The Story of American Tropical Medicine.**—pp. x+372. With numerous illustrations. 1942. New York: Henry Holt & Company, Inc. [21*s*.]

The subtitle of this book is *The Story of American Tropical Medicine*, and to those who like history served to them in the form of the historical novel the work will be very acceptable, for the main facts are accurate, though the mode of expression and the way in which they are presented will often jar on the ears of the British reader. It will appeal to medical men as well as to the laity, but rather to the latter for they will appreciate the familiar and chatty style of diction more than the former, who are accustomed to look on medical history as a subject to be treated in a serious vein.

In despite of these and other blemishes the book has much of value and should be widely read, because most of the facts are accurate and

clearly expressed. We do not know whether or not the author is a medical man. If he is not, he has a wonderful flair for grasping the important salient points of a scientific investigation; if he is, it is difficult to account for some glaring mistakes. Among the mistakes we note (p. 2), "The doctor made the conventional blood test. The concentration of *Sporozoa plasmodiiae* was frighteningly high." This is a new addition to the many synonyms of the malarial parasite. No medical man, certainly none with knowledge of tropical medicine, would report that he "found the zygotes of malaria in the blood of virtually every child examined" (p. 213). This peculiar statement concerning the presence of zygotes in a patient's peripheral blood occurs twice. Again (p. 19), the author speaks of "Bubonic plague, the louse-carried nemesis of medieval Europe."

Nevertheless the book has much merit and is consequently deserving of a critical review, and we pass on to deal with the individual chapters.

Chapter I gives a good general account of the difficulties to be overcome in achieving health in Latin-America, but overstatement detracts from rather than adds to the picture. The next chapter is interesting in telling of the rise of research institutions. Chapter III is mostly an account of Gorgas's achievements (enlarged upon later in Chapter VI giving his life-story) and those of his fellow-workers on the construction of the Panama Canal, but there is too little mention of the opposition of the administration against which he had to contend in the earlier days of the undertaking. Chapter IV, concerned in the main with the life of Carlos Finlay, contains also discussion of epidemics of earlier centuries. It is gratifying to the reviewer, who has repeatedly stressed the point, to see that the author gives due recognition to Finlay for his primary and fundamental idea of the Tiger mosquito as transmitter of yellow fever, on which the findings of the American Commission later were based. He states, however, that for purposes of immunization Finlay used "inoculation of blister serum from an active case," but makes no mention of his employing the more natural method of allowing infected mosquitoes to bite. Chapter V is a good life of Walter Reed, interesting to doctor and layman alike, but more, perhaps, to the latter because of its chatty style. The former would prefer a sober account of the facts, and the facts are all there. The chapter shows lack of arrangement; it starts with a description of Reed's grave, then of his work on typhoid fever and yellow fever and of the time when he was forty-nine; it then returns to his birth and records his life-history. This is somewhat marred, for British readers at least, by trivialities.

There is a mistake on p. 102 that Ross, in 1894, found in the Anopheles the unmistakable zygotes of malaria parasites. Mosquito Day, the actual date of the discovery, was August 20th, 1897. Chapter VI contains the fascinating story of Gorgas's life. His death, however, occurred at the Army Hospital, Millbank, not Willbank as is stated twice. Next follows an account of Deeks's life-work, good and interesting, but again somewhat spoiled by vulgarisms and hyperbole, such as: "They shake with chills and fevers. They curl up with brain clog They rot with blackwater fever. Amoeba bugs play leap frog down their guts" (p. 157). The life of Noguchi is very readable (Chapter VIII) but what may be called the terminal African period of his research life is rather slurred over—the reasons for his going to Africa, his chagrin at the non-acceptance of his *Leptospira icteroides*, first by

Agramonte, later by workers in West Africa. Noguchi was undoubtedly a wonderful man with an exceptional brain, but he was a bad loser and could not bear opposition.

Chapter IX is full of interest, and offers information on many diseases, among them smallpox, cholera, measles, typhus, whooping cough, tuberculosis, pneumonia, influenza, leprosy, dengue and dysentery, and on obstetrics and water supplies, all in 20 pages. Some of the *Fierce, deep, black mysteries* spoken of in Chapter X are mysteries no longer. Pinta, for example, is not a mysterious fungus disease; the author writes "I have examined about twenty of the fungi which are causative agents." Pinta, as was suggested many years ago, has now been shown to be due to a spirochaete. Chagas's disease is said to be "carried to man by mites, ticks, bedbugs and Triatoma . . . and perhaps other vermin" (p. 234), whereas the vectors are some of the Reduviid bugs. It is true that four species of bedbugs and three ticks have been experimentally infected, and the latter are capable of transmitting infection, but proof has yet to be produced that they do so in nature. Again, that American trypanosomiasis causes goitre is hardly any longer even problematical; all the evidence goes to show that goitre is not an essential part of the disease. Yet again he says "rat-bite fever . . . known principally in the West Indies" (p. 235). The chief country of rat-bite fever is Japan, where it is known as sodoku (so=rat, doku=poison); it is a rarity in the West Indies. The author speaks of "research among the mycoses and shytoses." The last is a new word to the reviewer; can he mean phytoses? On the next page we read, yaws "treatment is usually laborious and painful." We cannot understand the grounds for such a statement. On the contrary, in the vast majority of cases nothing is more dramatic than the results of treatment. Lesions may clear entirely within a fortnight and on an average three injections of the appropriate arsenical will bring about cure and in half the cases permanent cure. "Sprue," he says, "is the result of lowered vitality disordered digestion, constipation or diarrhoea; sallow complexion, lowered blood pressure, persistent loss of weight and, according to autopsy, of diminution in the size of the liver." If the wording is not faulty, the statement is. Sprue is certainly not the result of lowered blood pressure and diminution in the size of the liver. Under pellagra no mention is made of the work of SPIES, probably the greatest authority on this disease in America or elsewhere. The title of this chapter is not well chosen for, of the diseases mentioned and discussed in it, typhus, Chagas's disease, filariasis, dysentery, ankylostomiasis and tuberculosis can hardly be regarded as "deep, black mysteries." Of leprosy it is stated "Vaccines are proving at least partially effective"; chaulmoogra and its derivatives receive no mention. Chapter XI is good and well up to date, even to mentioning *Anopheles bellator*, which United States Army medical officers have comparatively recently shown to be an effective transmitter of malaria. More might be said on species sanitation and engineering projects, canalization and drainage, in prevention.

In a serious work on the history of tropical medicine, to find a chapter entitled *Damn the Mosquitoes!* brings one up with a jerk. Chapter XII relates the story of the United Fruit Company and its medical activities, and a fascinating story it is. The penultimate chapter touches upon a variety of subjects and, incidentally, contains several mistakes. The Nubian mountains (p. 301) doubtless mean the Nuba

Mountains in the Sudan, where there was recently so serious an outbreak of yellow fever. On the same page we find " During the First World War era, yellow fever . . . flared up fiercely . . . in Suez, Mesopotamia and Iraq," and " fourteen species [of mosquito] actually carry yellow fever " ; comment on these dicta are needless for those with knowledge of tropical medicine. Again, " blackwater fever, a malady which ravages liver and bladder cells " (p. 305) ; " one-third to two-thirds of all native people carry malaria zygotes in their blood streams" (p. 306). The old story, now known to be a fable, of the Countess of Chinchon is repeated as if it were factual. The history of Cinchona is much more interesting and even romantic than the author's bald version. The final chapter is political.

In a work on American tropical medicine we are surprised to find no mention of the epic struggles of those engaged in solving the problem of Rocky Mountain fever, nor of the work of Alice Evans on *Brucella abortus*.

There is a bibliography with a few references for each chapter and four appendices. The first is of acknowledgments, but only to American sources of information ; the second is another bibliography of 149 general references ; the third is a chronological list of some of the more important Latin-American epidemics with suggested places of origin ; the fourth quotes certain population returns for various years, from 1585 to the present. The earlier figures can only be pure guesswork.

We have dealt fully with this work because, if allowance is made for the slips alluded to, the book is instructive and full of interest. The author writes in the opening chapter that " this book attempts to tell the story of the men in white who have been our best ambassadors of goodwill to countries where most men are sick and where most sick people are without hope," and he has carried out his purpose conscientiously. The book is well got up, the print is clear, misprints are few, illustrations appropriate and photographs well reproduced. We wish it all the success it merits. *H. Harold Scott.*

We record with great regret the death on April 24th, 1943, of Professor WARRINGTON YORKE, M.D., F.R.C.P., F.R.S. Professor Yorke was a Sectional Editor of the *Tropical Diseases Bulletin* from 1912 to the time of his death.

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By the South Essex Recorders, Ltd., Ilford.

(434) Wt. P1676/260 1,725 5/43 S.E.R. Ltd. Gp. 432.

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